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RIBOFLAVIN DEFICIENCY IN HUMAN SUBJECTS

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AND

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AUGUSTA, GA.

The possible relation of riboflavin deficiency to certain manifestations of human pellagra has been of interest to investigators of various deficiency diseases for a number of years. During 1935 and 1936 at least four groups of observers [1] treated small groups of pellagrins with relatively minute doses of riboflavin with no evidence of curative effect. Our own experience with four patients treated with 3 mg. of lactoflavin a day for five days was entirely negative. Sebrell, Hunt and Onstott [2] observed no improvement in dogs with experimental blacktongue given relatively large doses of riboflavin by mouth. Nevertheless the close similarity of the mode of death of dogs with experimental riboflavin deficiency with that in fatal human pellagra and the constant finding of extreme fatty degeneration of the liver in the two conditions seemed to point to some significant relation.

No clinical sign of human riboflavin deficiency had been recognized until Sebrell and Butler [3] in 1938 called attention to the incidence of "cheilitis" in a number of patients maintained under experimental conditions on a diet poor in riboflavin; this condition was cured by riboflavin. The "cheilitis" described by Sebrell and Butler occurs frequently in endemic pellagra and has commonly been considered an accessory sign of the pellagrous syndrome. Stannus [4] many years ago described it as "marginal stomatitis." The lesions consist of redness, desquamation and finally ulceration of the lips at the mucocutaneous junction with fissures or "rhagades" at the corners of the mouth; either or both may be present. A number of Sebrell's experimental subjects presented these phenomena before any frank signs of pellagra were evident. The relation of these epithelial lesions to the dermatitis of pellagra is of considerable interest, particularly since it has been the common experience that "cheilitis" and dermatitis heal slowly under nicotinic acid therapy of pellagra while treatment with yeast or liver extract causes rapid involution. It has also been observed that cheilitis may develop while oral and neurologic manifestations of pellagra are being cured with nicotinic acid.[3] In some instances cure of rhagades has been observed in patients treated with nicotinic acid alone,[5] but here the question of increased appetite with consumption of large amounts of "pellagra-producing" food containing some riboflavin must be considered. Spies and the Vilters,[6] thought that pellagrous dermatitis in patients treated with nicotinic acid healed more promptly after the administration of large doses of riboflavin.

During the past three months six patients have been observed who showed evidence of possible riboflavin deficiency; five of these had definite signs of pellagra as well. Patient 2 was so ill that it was not considered justifiable to hold her under experimental conditions; patient 5 had diabetes and was in urgent need of control, so her diet was that required for regulation of her diabetes. The other four patients were kept on our standard pellagra-producing diet during the period of experimental therapy. Riboflavin used in treatment was the synthetic crystalline product furnished by Merck & Co., Inc., and "Lactoflavin" for injection was furnished by the Winthrop Chemical Company. An extract of liver prepared for intravenous use but lacking in hemopoietic activity was furnished by Parke, Davis & Co.

REPORT OF CASES

CASE 1.—J. A. M., a white man aged 34, was admitted Dec. 30, 1938, in severe alcoholic excitement. He was known to have been on a prolonged debauch and to have eaten little for about three weeks. There was a fine scaly dermatitis of the nasomalar grooves and alae of the nose as well as of the chin. There were deep radiating fissures at the corners of the mouth, and the lips were red and excoriated along the line of apposition. The tongue was typical of pellagra. There was slight brownish dermatitis of the hands and elbows. General physical examination as well as routine laboratory determinations showed nothing of significance. The gastric contents after histamine showed 20 degrees free hydrochloric acid and 30 degrees total acidity. He was maintained largely on dextrose solutions given intravenously and liquids by mouth for ten days, during which there was slight increase in the labial lesions and glossitis. There was no diarrhea. A pellagra-producing diet was begun Jan. 10, 1939, and on January 11, 12 and 13 the "nonhemopoietic" liver extract was given, 40 cc. intravenously each day. No effect on the glossitis or cheilitis was evident after six days. Lactoflavin was then administered

From the Department of Internal Medicine, University of Georgia School of Medicine and the University Hospital.

1. Dann, W. J.: Vitamin G Complex: Nonidentity of Rat Dermatitis Due to Vitamin B_6 Deficiency and Dermatitis of Human Pellagra, J. Nutrition **11**: 451-462 (May) 1936. Spies, T. D.: Personal communication to the authors. Fouts, P. J.; Lepkovsky, S.; Helmer, O. M., and Jukes, T. H.: Successful Treatment of Human Pellagra with "Filtrate Factor," Proc. Soc. Exper. Biol. & Med. **35**: 245-247 (Nov.) 1936. Authors' unpublished observations.

2. Sebrell, W. H.; Hunt, D. J., and Onstott, R. H.: Lactoflavin in Treatment of Canine Blacktongue, Pub. Health Rep. **53**:235 (Feb. 26) 1937.

3. Sebrell, W. H., and Butler, R. E.: Riboflavin Deficiency in Man, Pub. Health Rep. **53**: 2282 (Dec. 30) 1938.

4. Stannus, H. S.: Pellagra in Nyasaland, Tr. Soc. Trop. Med. & Hyg. **5**: 112-119, 1912.

5. Smith, T. D.: Personal communication to the authors. Authors' present report.

6. Vilter, R. W.; Vilter, S. P., and Spies, T. D.: Relation Between Nicotinic Acid and a Codehydrogenase (Cozymase) in Blood of Pellagrins and Normal Persons, J. A. M. A. **112**: 420-422 (Feb. 4) 1939.

intramuscularly, 3 mg. a day from the 19th through the 24th. January 23 there was definite evidence of healing of the lips. This continued slowly and was complete on the 30th. During the same time the scaly dermatitis of the nose and chin resolved. Later treatment with nicotinic acid caused rapid cure of the glossitis.

CASE 2.—R. B., a white woman aged 38, was admitted Jan. 3, 1939, with a diagnosis of severe endemic pellagra. She was emaciated, disoriented and slightly febrile and had severe diarrhea. There was marked fine scaly dermatitis of the nose and malar eminences without erythema. The lips showed extreme redness and excoriation along the line of closure, and there were deep radiating fissures at the corners. The gums, oral mucosa and tongue were fiery red with much superficial ulceration and gray exudate, the pharynx and visible portions of the larynx showed similar lesions and the patient was aphonic from involvement of the vocal cords. General physical examination revealed nothing noteworthy. The vagina was intensely red with much seropurulent discharge. Dermatitis of the neck, hands and feet was absent. The blood showed 10 Gm. of hemoglobin per hundred cubic centimeters, 4,100,000 erythrocytes and 7,600 leukocytes per cubic millimeter. The Wassermann reaction was strongly positive. Other laboratory examinations were not significant. It was not possible to examine the gastric contents on account of the extreme sensitiveness of the inflamed pharynx. The patient was given a soft pellagra-curative diet without yeast, and nicotinic acid was administered intravenously, 300 mg. a day from January 4 to 7; thereafter it was given by mouth, 75 mg. a day. There was the usual dramatic response of the glossitis, stomatitis and diarrhea; all were cured on the third day of treatment, and on this day the mental state seemed quite normal. The patient ate of the curative diet greedily after the first day of treatment. The lips healed somewhat more slowly than the buccal mucosa, but on the fifth day of treatment cheilitis and rhagades were cured.

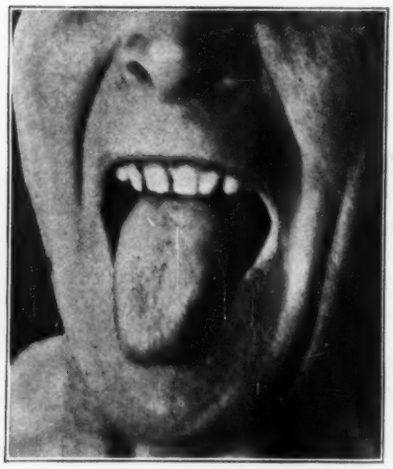

Fig. 1 (case 3).—Tongue on admission.

Fig. 2.—(case 3).—Dermatitis of hands on admission.

CASE 3.—F. P., a white man aged 54, was admitted Feb. 9, 1939, with a diagnosis of relapse of chronic pellagra; he had been seen on four previous admissions with severe pellagrous lesions. At this time there was slight branny desquamation of the nose and malar eminences, the lips and buccal mucosa were of normal color, there were no fissures at the corners of the mouth and the tongue was of normal color and texture (fig. 1). The hands showed a bright red "dry" dermatitis with marked desquamation (fig. 2) quite different from the usual vesicular and bullous lesions present on previous admissions and the genitalia and feet were free from dermatitis. General physical examination was negative. The blood contained 11 Gm. of hemoglobin per hundred cubic centimeters and 3,000,000 red cells and 11,000 white cells per cubic millimeter. There was total achlorhydria after histamine. Other laboratory examinations were not significant. This man was of particular interest because he had been the subject of numerous therapeutic experiments and was a very labile pellagrin in whom relapse could be produced quite regularly by maintenance on dextrose and water or on a "maize diet" for five or six days. His present dermatitis was quite different from that seen on previous admissions; the usual severe stomatitis and glossitis were absent and he did not have diarrhea. He was given the basal pellagra-producing diet and riboflavin was administered subcutaneously, 50 mg. February 12, 13 and 14. No other treatment was used and from February 15 the left hand was exposed to an infra-red lamp for twenty minutes twice each day. On February 16 there was definite blanching of the hands; this was progressive and by February 24 the skin was of normal color, though there was still some desquamation. In the opinion of various observers the hand exposed to heat healed somewhat more rapidly than did the other. February 27 an attempt to produce relapse was made by putting the patient on a dextrose and water diet; this was continued for five days with no effect (fig. 3). A "maize diet" consisting of 500 Gm. of cornmeal mush and syrup as desired was then substituted for dextrose and water and continued for four days without producing any sign or symptom of pellagra. The experiment was then terminated.

Fig. 3 (case 3).—Hands after treatment with riboflavin.

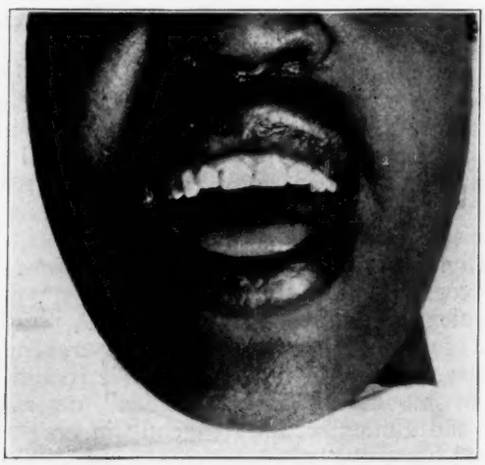

Fig. 4 (case 4).—Lesions of lips and nares before treatment.

CASE 4.—L. J., a Negro girl aged 17, was seen Feb. 18, 1939, on account of a "sore mouth" which had developed during hospitalization subsequent to an arthroplasty of the left hip joint. For about three weeks after the operation she had refused regular ward diet and had eaten hardly anything except white bread and syrup, corn bread and syrup and hominy with gravy. She was excellently nourished and developed, afebrile and free from gastrointestinal disturbances. The palpebral and scleral conjunctivas were very red, there was a small amount of serous exudate from the conjunctival sacs, and photophobia was extreme. There was no evidence of iritis. The lips were intensely red, almost denuded, with deep fissures in the vermilion and slight fissures at the corners; the upper lip showed an oozing moist dermatitis; there was a deep fissure

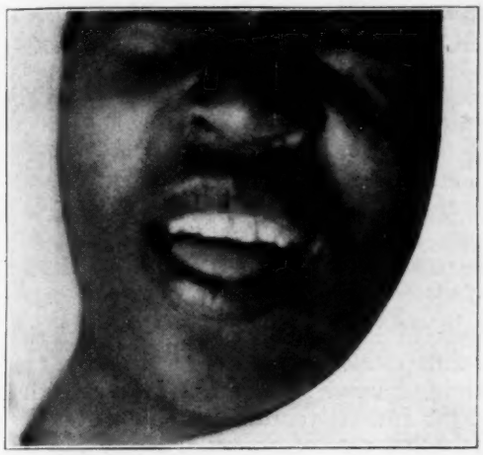

Fig. 5 (case 4).—Lips and nares after treatment with riboflavin.

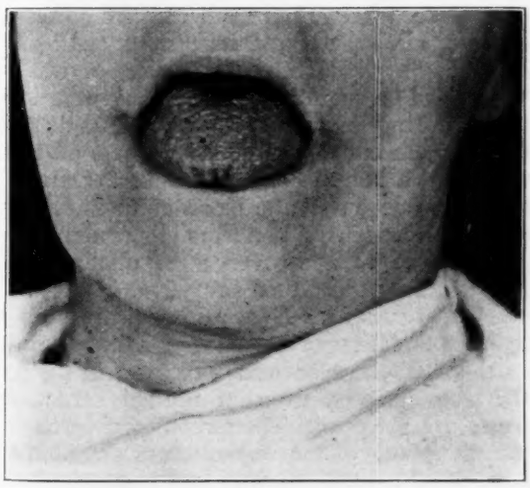

Fig. 6 (case 5).—Lesions of lips and corners of mouth on admission.

at the junction of the nasal septum and lip, and the septum and lower portions of the alae showed dermatitis similar to that on the upper lip. The skin elsewhere was of excellent texture. The tongue and buccal mucosa showed nothing abnormal. General physical examination and routine laboratory procedures were not significant. Cultures from the lips and nose showed no unusual bacteria and no fungi (fig. 4). The patient was put on a pellagra-producing diet, which she ate well, and on February 19 riboflavin was given by mouth, 30 mg. in doses of 10 mg. three times a day; this was continued until February 23. During these five days there was some improvement in the lips but none in the nasal lesion; the amount of riboflavin was increased to 60 mg. a day on February 24, and this dose was continued until February 26, at which time the lips were cured and the deep fissure at the base of the nasal septum was almost healed. Two days after treatment was discontinued there was a rapid recurrence of cheilitis and the nasal fissure reopened. On March 1 and 2 riboflavin was given hypodermically in doses of 10 mg. once a day, and by March 4 the lesions were again healed; on this occasion there was marked improvement in conjunctivitis and photophobia. On March 9 a second relapse occurred, the lips nose and conjunctivas being quite as much affected as at first. On this day 20 mg. of riboflavin was given intravenously. From this time on there was rapid healing of the lips and nose with disappearance of conjunctivitis and photophobia. On

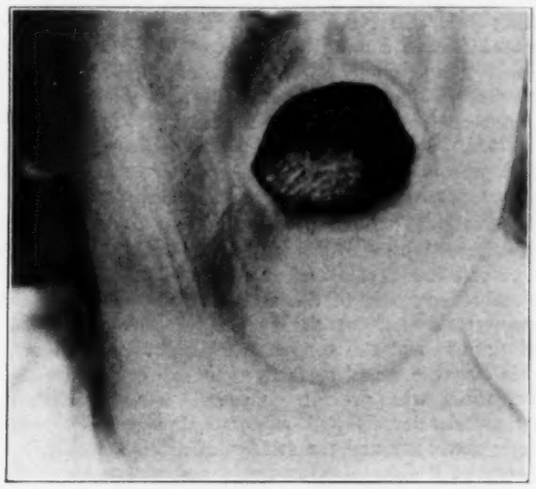

Fig. 7 (case 5).—Lips after treatment with riboflavin.

March 15 no abnormality of the lips could be seen, the nasolabial fissure was healed and the eyes were normal (fig. 5). The patient was then given a regular diet and has remained well.

CASE 5.—M. W., a white woman aged 58, was admitted March 1, 1939, with the diagnosis of diabetes mellitus. She was slightly obese, somewhat pale and had slight edema of the feet. There were deep fissures at the corners of the mouth, and the lips were red and slightly excoriated along the line of apposition (fig. 6). The tongue was bright red, atrophic and fissured. General physical examination showed cardiac hypertrophy, severe hypertension and moderate enlargement of the liver. There was vaginitis with some seropurulent discharge. The fasting blood sugar was 330 mg. per hundred cubic centi-

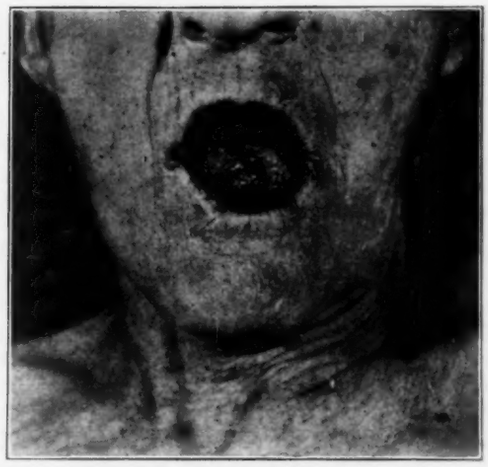

Fig. 8 (case 6).—Lesions of corners of mouth which developed during treatment with nicotinic acid.

meters, and 11 Gm. of dextrose was excreted in the first twenty-four hour collection of urine. She was given a diet containing 50 Gm. of protein, 50 Gm. of fat and 150 Gm. of carbohydrate, and 10 units of protamine zinc insulin was administered each morning. On the third day the lips were healed and the fissures at the corners of the mouth were dry and well covered with epithelium. The original amount of protamine zinc insulin was found inadequate and the dose was increased on March 8

to 30 units. On March 10 the fissures at the corners of the mouth reopened and were quite painful; the tongue had remained red and fissured. On March 11 riboflavin was given intravenously, 10 mg. in 200 cc. of physiologic solution of sodium chloride, and on March 12, 25 mg. was administered by the same route. The lips healed during the ensuing three days and the patient felt much better; no change was noted in the tongue (fig. 7). During this time the dose of insulin had been increased to control glycosuria and hyperglycemia until 50 units was being given daily. March 19 there was a sudden recurrence of the cheilitis and painful fissures at the corners of the mouth. Riboflavin was given by mouth in doses of 20 mg. a day for five days, and again the lips healed, though small fissures persisted in the right corner of the mouth. Nicotinic acid was then started, 25 mg. four times a day. Glossitis, which had persisted, was healed on the third day of treatment, but slight excoriation persists at the corners of the mouth.

CASE 6.—L. H., a white woman aged 68, was admitted March 8, 1939, with the diagnosis of chronic endemic pellagra. She was emaciated, pale and slightly disoriented. There was slight scaly dermatitis of the nose and nasolabial folds, small fissures were present at the corners of the mouth, the lips seemed normal and the tongue was bright red and atrophic. The skin over the dorsal surfaces of the hands was atrophic but no dermatitis was present. General physical examination showed arteriosclerosis and moderate hypertension, moderate cardiac hypertrophy and the residua of a left hemiplegia. The blood showed 9 Gm. of hemoglobin per hundred cubic centimeters, 3,800,000 red cells and 8,400 white cells per cubic millimeter. The gastric contents were achlorhydric. The patient had been seen on several occasions with various manifestations of pellagra. She was given a pellagra-producing diet, and nicotinic acid was administered intravenously, 100 mg. a day from the day of admission until March 20. Disorientation and glossitis were absent on the third day of treatment but the fissures at the corners of the mouth grew rapidly worse and by March 11 were so painful as to interfere with eating (fig. 8). Ten mg. of riboflavin was given subcutaneously on March 11, and because no effect was observed 50 mg. was given by the same route on March 13. On the second day there was much improvement in the oral fissures but by March 17 they had recurred and were painful. Riboflavin was then given by mouth, 20 mg. daily from March 17 to March 23, with some improvement. The fissures became dry and less painful but did not heal. March 20 a soft diet was given and oral administration of 100 mg. of nicotinic acid was substituted for intravenous injection. During the nine days no change has occurred in the fissures at the corners of the mouth, though there has been considerable improvement in the patient's condition.

COMMENT

Five patients who presented lesions corresponding with those described by Sebrell and Butler as being due to riboflavin deficiency have been observed; another with atypical dermatitis of the hands is included in this report. Five of these patients either showed evidences of pellagra or were known to be chronic pellagrins. Patient 2 was cured of cheilitis as well as of pellagrous lesions while under treatment with nicotinic acid and an ample diet. It seems likely that adequate intake of food containing ample amounts of riboflavin explains her recovery. Patient 4 had no sign or symptom of pellagra but showed severe cheilitis and conjunctivitis; she recovered under riboflavin, given by various routes, and twice relapsed soon after treatment was discontinued. Patient 3, who was a known pellagrin, showed no definite signs of pellagra but had an atypical dermatitis of the hands, which was apparently cured by large doses of riboflavin. Attempts to produce pellagra by severe dietary restriction were later unsuccessful. The other three patients showed much improvement of cheilitis and fissures in the corners of the mouth under riboflavin therapy, though there was a tendency to rapid relapse when treatment was stopped. Large doses of riboflavin were much more effective in all cases and parenteral administration seemed much more efficient than oral. In every instance response to riboflavin was relatively slow, and in the presence of an inadequate diet nicotinic acid given concurrently seemed to have no adjuvant effect. One patient developed cheilitis while under treatment with nicotinic acid.

Particular interest was aroused by cases 3 and 4, in which dermatitis, cheilitis and conjunctivitis seemed to be cured by riboflavin.

A NEW METHOD OF TREATMENT OF SUBACUTE BACTERIAL ENDOCARDITIS

USING SULFAPYRIDINE AND HEPARIN IN COMBINATION: PRELIMINARY REPORT

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WITH THE ASSISTANCE OF

PAUL D. WHITE, M.D.

BOSTON

Analysis of 250 cases of subacute bacterial endocarditis with positive blood cultures for alpha (viridans) and, rarely, gamma streptococci in Boston hospitals[1] stressed the ineffectiveness of all varieties of therapy prior to the new chemotherapeutic drugs. Sulfanilamide, used in twenty-four cases, and prontosil, used in five, temporarily improved a few; used in four cases, sulfapyridine, although not curative, appeared far more effective. Data that we have collected from other clinics and from one case report concerning sixty-six well studied cases in which intensive treatment was given with sulfapyridine confirm our experience that in most instances the drug lowers the temperature and sterilizes the blood stream but that these effects pass off in from a few days to a month or, rarely, more. Only in one reported case,[2] in which the blood cultures were positive for gonococcus and a nonhemolytic anaerobic streptococcus, was there a recovery; the disease followed its usual course in the other sixty-five.

Blood of patients with subacute bacterial endocarditis usually has a high titer of antibodies for the organisms;[3] despite this fact, these bacteria will grow in the serum, but they die quickly, even in normal serum, when leukocytes are present.[4] The streptococci lie as a rule near the periphery of the vegetation, a mass chiefly of fibrin, an ideal culture medium and protective barrier, and of platelets. Polymorphonuclear leukocytes are scarce or absent in the vegetation.[5] At its base, fibrosis is a nearly constant finding.

By present means it appears impossible to increase the number of phagocytes and draw them into contact with the bacteria, to dissolve the vegetations or to induce granulation within them. One can attempt, however, to prevent further thrombotic deposition on their surface in order to (1) restrict the nidus and culture

From the Medical Department (Cardiac Laboratory) of the Massachusetts General Hospital.

1. Kelson, S. R., and White, P. D.: The Diagnosis, Prognosis, and Treatment of Subacute Bacterial Endocarditis, to be published.
2. Orgain, E. S., and Poston, M. A.: Gonococcal Endocarditis, with Recovery After Sulfapyridine, New England J. Med. **221**: 167 (Aug. 3) 1939.
3. Kinsella, R. A.: Bacteriological Studies in Subacute Bacterial Endocarditis, Arch. Int. Med. **19**: 367 (March) 1917. Wright.[5]
4. Friedman, Meyer; Katz, L. N., and Howell, Katherine: Experimental Endocarditis Due to Streptococcus Viridans: Biologic Factors in Its Development, Arch. Int. Med. **61**: 95 (Jan.) 1938.
5. Wright, H. D.: The Bacteriology of Subacute Infective Endocarditis, J. Path. & Bact. **28**: 541 (No. 4) 1925.

medium for bacterial growth, (2) prevent embolism from the freeing of fresh thrombus, and (3) check the growth of the vegetations so that proliferating fibroblasts may fill in the areas thus limited.

These considerations have led us to treat the disease not only with sulfapyridine, for its bacteriostatic and perhaps bactericidal action,[6] but also with an anticoagulant, crystalline heparin,[7] which had been shown effective and in other conditions nontoxic, was chosen.[8]

METHOD

The contents of a 10 cc. vial of heparin (10,000 units) is added to 500 cc. of physiologic solution of sodium chloride, and such a solution is given by uninterrupted intravenous drip day and night for fourteen days. The rate of flow (usually from 15 to 25 drops a minute) is carefully regulated to maintain, as well as possible, the venous clotting time (normally below twenty minutes) at approximately one hour. Clotting time is measured before treatment, twice or more the first day and then at least daily by the five tube method of Lee and White.[9] Heparin is begun from four to seven days after sulfapyridine has been started, when nausea and vomiting have subsided and before "escape" from its effects has occurred. From 4 to 6 Gm. of sulfapyridine (with desired blood levels of 5 mg. per hundred cubic centimeters or more) is given daily by mouth before and during the use of heparin and for one week afterward—a total of about four weeks. Blood transfusions are given if there is anemia of 3,500,000 red blood cells or below. Persisting infections (including this one[1]) predispose to vitamin C deficiency,[10] which interferes with fibrous repair;[11] all patients, therefore, are saturated with 200 mg. of ascorbic acid by mouth four times a day for three days and continued on 100 mg. a day. Other added vitamins and iron are not essential to the therapy.

RESULTS

Six of our patients with subacute bacterial (Streptococcus viridans) endocarditis and one patient with the rarer condition of acute bacterial endocarditis caused by the same organism have received the combination of sulfapyridine and heparin. Each had had four or more positive blood cultures. They were treated in the following order:

CASE 1.—F. G., a man aged 21 with advanced disease complicating patency of the ductus arteriosus, had severe recurrent pulmonary infarction after three days of heparin (April 1939) and both drugs were omitted. He died two weeks later.

CASE 2.—E. S., a man aged 22 with a history of five attacks of rheumatic fever, resulting in great heart damage, had been ill two and one-half weeks with characteristic manifestations of subacute bacterial endocarditis. Because of a red tender joint, migratory arthralgia, prolonged auriculoventricular conduction and epistaxes, concurrent rheumatic fever was diagnosed[12] and further indicated by later onset of auricular fibrillation following rheumatic pleuritis. The rectal temperature (104.6 F.) fell sharply on administration of sulfapyridine (April 1939); cultures became negative. He was given two transfusions. After receiving a total of 260 cc. of heparin in fourteen days he gained strength and weight, and his temperature stayed under 100 F. for forty-five days (except for one rise of 0.5 degree F.), then rose for three days with the pleuritis. Since then, signs of rheumatic infection have recurred, and he has been kept in bed since fibrillation appeared, with persistent congestive heart failure. He has shown no evidence of bacterial endocarditis, however, since shortly after the specific treatment was stopped; since sulfapyridine has been omitted (May 19) nineteen consecutive blood cultures have been negative.[12a]

CASE 3.—A. C., a woman aged 23 with rheumatic fever at 9 years and a slight mitral lesion, had a slowly progressing bacterial endocarditis for six months, with an oral temperature to 102 F. and splenic and cerebral embolism. Blood cultures became negative on administration of sulfapyridine (April 1939). She received 290 cc. of heparin in fourteen days. Since sulfapyridine has been omitted (May 26) all blood cultures have been negative, she has gained strength and weight (26½ pounds [12 Kg.] in three months) and has shown no evidence of the disease. She has walked since June 14, is active and at work and has no complaints.

CASE 4.—M. S., a girl aged 19 years, with three attacks of rheumatic fever and severe heart damage, had been ill three weeks. After two transfusions, sulfapyridine was begun (June 1939; the rectal temperature fell sharply from 102-104 to 100 F. or less but rose after eight days. Cultures remained positive. Heparin was omitted after forty hours because of sudden headache, vertigo and amblyopia. These conditions cleared, but five days later, after thirteen hours of heparin, she had a chill and fever and died. Autopsy showed large occipital and subdural hematomas. These were probably embolic and occurred, we believe, spontaneously, though the drug very likely increased the hemorrhage and hastened death.

CASE 5.—E. L., a man aged 41 with rheumatic aortic and mitral regurgitation, entered the hospital July 8, 1939, because of chills, high fever and prostration for one week following six weeks of malaise. The rectal temperature of 104.5 fell to normal on administration of sulfapyridine but rose after two days; blood culture remained positive. An hour and a half after beginning heparin he had a chill and high fever and went into collapse. He died seventeen hours later. Autopsy showed the typical lesion of acute bacterial endocarditis on the aortic valve. His reaction after administration of heparin, and the reactions in cases 6 and 7 were later traced to a faulty lot of the drug, which caused similar reactions in several patients with other conditions. Such reactions had not occurred previously and have not occurred since.

CASE 6.—R. M., a man aged 25 with well borne aortic regurgitation, which followed rheumatic fever at the age of 8 years, entered the hospital July 21, 1939, with bacterial endocarditis of one week's duration. The temperature fell to normal on sulfapyridine and blood cultures became negative. A chill and high fever occurred after one and one half hour's use of heparin of the same toxic lot as that noted in case 5 and after two further trials of the drug. He was therefore continued as a control case on sulfapyridine alone, but emboli occurred from time to time, anemia progressed, fever recurred and a blood culture, taken thirty-eight days after treatment was started, was positive. Ten days later sulfapyridine was discontinued and a new lot of heparin was begun without reaction; to date there has been little change in his condition.

CASE 7.—J. H., a man aged 41 with well compensated mitral regurgitation following rheumatic fever at 16, entered the

6. Marshall, E. K.: Bacterial Chemotherapy: The Pharmacology of Sulfanilamide, Physiol. Rev. **19:** 240 (April) 1939 (see pp. 255-258). Keefer, C. S., and Rantz, L. A.: Sulfanilamide; A Study of Its Mode of Action on Hemolytic Streptococci, Arch. Int. Med. **63:** 957 (May) 1939.

7. Heparin is obtained from the Connaught Laboratories, University of Toronto, Toronto, Canada, at a cost of $2.72 a vial.

8. Murray, D. G. W., and Best, C. H.: Heparin and Thrombosis: The Present Situation, J. A. M. A. **110:** 118 (Jan. 8) 1938; The Use of Heparin in Thrombosis, Ann. Surg. **108:** 163 (Aug.) 1938. Mason, M. F.: Heparin: A Review of Its History, Chemistry, Physiology and Clinical Applications, Surg. **5:** 451 (March) 1939; **5:** 618 (April) 1939.

9. Hunter, F. T.: Laboratory Manual of the Massachusetts General Hospital, Philadelphia, Lea & Febiger, 1939, p. 25.

10. Faulkner, J. M.: The Effect of Administration of Vitamin C on the Reticulocytes in Certain Infectious Diseases, New England J. Med. **213:** 19 (July 4) 1935.

11. Lanman, T. H., and Ingalls, T. H.: Vitamin C Deficiency and Wound Healing, Ann. Surg. **105:** 616 (April) 1937.

12. White, P. D., and Kelson, S. R.: The Clinical Relations Between Subacute Bacterial Endocarditis and Rheumatic Fever, to be published.

12a. This patient died in congestive failure Oct. 12, 1939. Autopsy revealed an area of clearcut definitely healed bacterial endocarditis with typical vegetations, fibrous and calcified, on the chronically scarred (rheumatic) mitral valve. This healed lesion is consistent in time relationship with apparently effective treatment six months earlier. The aortic valve showed also extensive rheumatic scarring, but without any vegetations of bacterial endocarditis. The myocardium is being examined for Aschoff bodies.

hospital July 20, 1939, severely ill with bacterial endocarditis of seven months' duration. The rectal temperature, which had been spiking to 103 F., fell to normal, and blood cultures became negative following the use of sulfapyridine. He received two transfusions. Heparin of the same toxic lot noted in case 5 was begun but omitted after one hour because of a chill and fever. On the eighteenth day of sulfapyridine medication, heparin of another lot was resumed without reaction; he received 185 cc. over a seven and one-half day period (a larger supply was then lacking). Sulfapyridine was continued for two weeks longer, until September 7. His improvement has been striking. He began to walk four days later (after having been bedridden for three months) and still remains free of evidence of the disease, four weeks after stopping treatment.

Sulfapyridine was continued despite nausea and vomiting, which were severe in two cases; these symptoms gradually subsided. Lymphangitis in the region of the intravenous injection in two cases cleared with change of the site of injection and hot packs.

COMMENT

We have administered sulfapyridine and heparin to six patients with subacute and one patient with acute Streptococcus viridans endocarditis. Two of these patients, one with subacute (patient 6) and one with acute (patient 5) endocarditis, were able to take the heparin for only an hour and a half because of reactions to a toxic lot of the drug, too short a time to expect any lasting effect on thrombus formation. Two other patients (1 and 4) were able to continue the heparin for only three days and two days respectively because of the serious course of the disease itself, which terminated fatally in a short time (two weeks or less).

The remaining three patients were able to take the heparin for more than a week, a length of time probably adequate to produce an important effect on thrombus formation. All these three patients showed striking improvement and have been free from evidences of the disease for nineteen weeks, eighteen weeks and four weeks respectively after discontinuing treatment. With these results we contrasted 246 follow-up control cases: afebrile intervals were rare for as long as five weeks once fever had set in, and no patient, so far as we could determine, remained free from signs and symptoms for that length of time except one boy, who without specific therapy did so for a full year before he died of rheumatic fever.[13] Our three subjects, moreover, lack the characteristics of "bacteria-free" cases.[14]

We recognize the possible danger of excessive bleeding incident to embolism in these cases but believe it fair to accept this risk in the face of the hopeless prognosis of the disease. The chances of healing the vegetations would seem best early in the disease when they are small. In this infection, in which exacerbations with crippling and fatal embolism strike suddenly, the earliest possible diagnosis and an attempt at early therapy are important.

The treatment which we have recounted is new and still in the experimental stage; it is not to be advised except under close and careful observation and preferably in the earlier cases or less seriously ill, and there must be no doubt about the diagnosis. It can do harm, but the possible benefit may well outweigh the risks, we believe, in this almost universally fatal disease. Time will show how much more effective, if any, the combined sulfapyridine and heparin therapy may be than the use of either drug alone; there are likely to be infrequent recoveries from the administration of the single drug sulfapyridine or even sulfanilamide; heparin has not yet, so far as we know, been employed alone in the treatment of this disease. Neither blind to the failures nor prematurely boastful of the apparent successes, we shall continue patiently to gather further experience to learn just how good our combined therapy may prove to be and to better its technic. This preliminary report is presented because of the interesting method of attack and because that attack has in these first few months given more promise than any other method that we have ourselves used or heard of in the past.

13. In a recent article Dr. Joseph A. Capps (Subacute Bacterial Endocarditis Due to Streptococcus Viridans with Special Reference to Prognosis, Ann. Int. Med. **13**:280 [Aug.] 1939) states that he has seen no recovery from subacute bacterial endocarditis since 1924. Kelson and White.[1]

14. Libman, Emanuel: A Consideration of the Prognosis in Subacute Bacterial Endocarditis, Am. Heart J. **1**: 25 (Oct.) 1925.

USE OF HEPARIN IN SUBACUTE BACTERIAL ENDOCARDITIS

A PRELIMINARY REPORT

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SAN FRANCISCO
W. W. HAMBURGER, M.D.
AND
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Recent studies from this department[1] on experimental Streptococcus viridans endocarditis in dogs indicated clearly that the infection persisted because the constant deposition of platelets and fibrin on the vegetation exceeded the rate at which the vegetation implanted on the valve could be sterilized. Further studies on both dogs and human beings suffering from subacute endocarditis of the Streptococcus viridans variety revealed that the blood did not lack the ability to destroy the organism in vitro and that its inability to do so in vivo was due to the fact that the effective agent in the blood, the white blood cell, was unable to reach the focus of infection because of the relative avascularity of the valve leaflets and the dynamics of the blood stream flowing past the vegetations.

Because of these facts it was thought possible that the prevention of new fibrin and platelet formation by the use of an anticoagulant might allow the valvular processes of repair and sterilization to gain the ascendancy and thus terminate the infection.

With this in mind, a patient was treated with new concentrated heparin, which has been shown by Murray, Jaques, Perrett and Best[2] to be effective in the prevention of thrombosis in animals and possibly in man, following surgical procedures. These workers have given this heparin by continuous intravenous infusion for days to many patients with no noticeable ill effects.

The following case report deals with our observations on a single patient having subacute bacterial endocarditis, who died of cerebral hemorrhage before the treat-

From the Cardiovascular Department, Michael Reese Hospital.
Read by title at the Central Society for Clinical Research, Chicago, during November 1938.
The cost of the heparin was defrayed by a grant from an anonymous benefactor. Dr. Best, Dr. Murray and their associates informed us concerning the utilization of heparin. Mr. Hutchison, of the Connaught Laboratories, cooperated in facilitating the shipments of heparin.

1. Friedman, Meyer; Katz, L. N., and Howell, Katharine M.: Experimental Endocarditis Due to Streptococcus Viridans, Arch. Int. Med. **61**: 95 (Jan.) 1938. Friedman, Meyer: A Study of the Fibrin Factor in Its Relation to Subacute Endocarditis. **63**:173 (June) 1938.

2. Murray, D. W. G.; Jaques, L. B.; Perrett, T. S., and Best, C. H.: Surgery **2**: 163 (Aug.) 1937.

ment had been continued sufficiently long to evaluate the worth of the procedure:

REPORT OF CASE

History.—A. H. was admitted to the Michael Reese Hospital March 5, 1938, complaining of weakness, fever, loss of weight and loss of appetite of several months' duration. His illness began insidiously in October 1937 with a vague feeling of malaise, and as it progressed there developed a continuous fever, loss of weight and strength, and embolic accidents. Before coming to the hospital, he had been unsuccessfully treated with quinine, sulfanilamide, antistreptococcus serum and blood transfusions. The essential pathologic changes on admission were (1) evidence of weight loss, (2) anemia, (3) clubbing of the fingers, (4) a Corrigan pulse with a capillary pulse, (5) an enlarged heart with a diastolic murmur at the base and a short systolic murmur at the apex and (6) a temperature and pulse rate elevation.

Laboratory examination revealed hemoglobin 65 per cent, red blood cell count 3,150,000, white blood cell count 12,500, sedimentation time 44 mm. in an hour, Weltman reaction 5, blood sugar 88, nonprotein nitrogen 35, occasional red blood cells in the urine, normal stool, Streptococcus viridans in three successive blood cultures, and evidence of myocardial damage shown in an electrocardiogram.

Following a blood transfusion, the new concentrated heparin was added to physiologic solution of sodium chloride and 5 per cent dextrose solution so that each liter contained 30,000 units of heparin. A needle was fixed in the vein and, by means of a rectal drip, the solution was given continuously for ten days. The coagulation time of the blood was maintained after the second day of treatment at twenty-five to thirty minutes (five times normal for this patient).

The intravenous heparin treatment was begun on March 8 and was discontinued on the morning of March 18 because the patient at this time began to show projectile vomiting. At the same time his blood pressure began to rise and his temperature to fall, suggesting a cerebral hemorrhage. He gradually lost consciousness and in the afternoon he died. In the ten days during which he received treatment he experienced

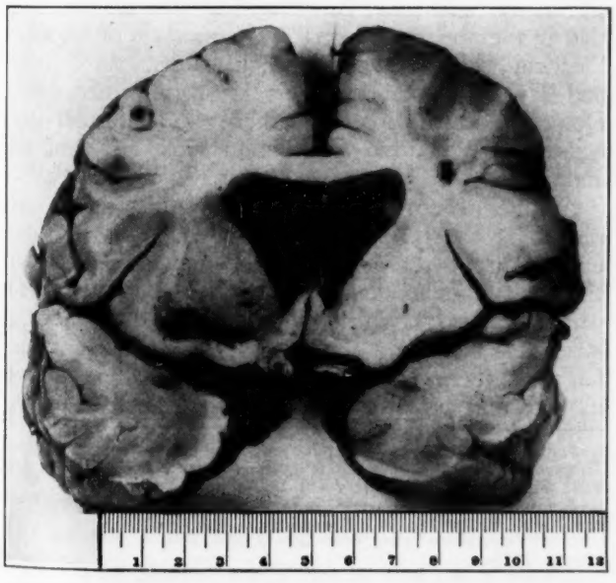

Fig. 1.—Section of brain showing encephalomalacia and hemorrhage into ventricles.

no symptoms other than a transitory diarrhea until the final episode. No petechiae were observed during the hospital stay. No hemorrhage was noted following the withdrawal of the intravenous needles, if pressure was applied for a few seconds.

Autopsy (by Dr. Otto Saphir).—There was no evidence of internal hemorrhage in any organ other than the brain. In this organ the lateral ventricles and the third and fourth ventricles were seen to be filled with blood and there was some blood in the subarachnoid space. The source of this hemorrhage was found to be an area of encephalomalacia (fig. 1) in the frontal lobe that had probably resulted from a previous infected embolus from seven to ten days before. The heart, particularly the left ventricle, was enlarged. The tricuspid and pulmonic valves were normal but the mitral and aortic valves showed an old healed endocarditis, and the aortic valve leaflets were seen to be the site of a vegetative process that had partially ulcerated the leaflets (fig. 2). The size of the vegetations on the leaflets were not large and were "clean"

Fig. 2.—Appearance of aortic valve showing ulcerative vegetations.

in appearance. There were two necrotic areas on the vegetations, possibly indicating dissolution of some of the fibrin. Immediately beneath the aortic valves on the wall of the left ventricle there was a minute vegetation, arising apparently by contact. There were several infarcts in the spleen in various stages of healing. The kidneys appeared normal grossly.

Microscopic sections of the brain lesion confirmed the opinion made from the gross examination. The aortic leaflet vegetations were observed to be fairly well organized, bacteria being present in the outer fringe of the thrombus, which had not yet become organized. No polymorphonuclear leukocytes in the valvular area immediately adjacent to the vegetation were observed. Small focal accumulations of round and polymorphonuclear cells were found in the myocardium. The kidneys showed an acute, disseminated glomerular nephritis.

COMMENT

We are placing this note on record in order to stimulate further clinical investigation of this method of therapy in subacute bacterial endocarditis. We are aware that there are theoretical dangers to its use, since in a disease prone to hemorrhage, as subacute bacterial endocarditis occasionally is, the use of heparin by interfering with the physiologic process of clotting may lead to intractable or even fatal hemorrhage following the rupture of a blood vessel after embolization, as might have occurred in this case. The sudden liberation of large quantities of bacteria should the vegetation disintegrate may cause an overwhelming bacteremia. The acute glomerular nephritis found in this case might have been caused conceivably by the heparin. Further, it has not been shown conclusively that heparin actually prevents the deposition of platelets and fibrin in man, although the evidence is highly suggestive. It is possible too that the promptness of instituting treatment becomes an important and vital factor. However, these contraindications to the use of heparin are not sufficient to discourage its use, since the disease itself is almost inevitably fatal and the possibility exists that some definite good may result. We therefore feel that the further trial of heparin in subacute bacterial endocarditis is warranted. Further studies are being projected in this department both on the experimental animal and on human beings.

THE BACTERIOSTATIC AND ANTITOXIC ACTIONS OF SULFANILAMIDE

TISSUE CULTURE STUDIES

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The bacteriostatic theory explains the curative effects of sulfanilamide in infections in small laboratory animals as due primarily to the bacteriostatic action of the drug. As a consequence of the reduced number of organisms, there is secondary reduction in the elaboration of toxic substances (leukocidin, hemolysin and the like). The theory states that under these conditions the natural defense mechanism of the body frees the tissues of the infecting organisms.

Bliss and Long,[1] basing their conclusion chiefly on the results of experiments with mouse peritonitis caused by the Welch bacillus, reported that the only demonstrable effect of sulfanilamide on this organism was bacteriostasis. Gay and Clark,[2] working with rabbit empyema caused by a hemolytic streptococcus of human origin, concluded that the primary effect of the drug was bacteriostasis.

Colebrook, Buttle and O'Meara[3] had earlier noted that the blood and serum of human beings and laboratory animals possessed increased bacteriostatic and bactericidal power after the administration of sulfanilamide and the prontosils. They regarded it as probable that this factor might be important in human infections but expressed surprise that the very low bactericidal power of the blood of mice should be associated with such marked curative effect.

Osgood[4] reported early in 1938 that the major effect of sulfanilamide appeared to be toxin neutralization. However, his conclusion was promptly criticized. In an exchange of papers, Hemmens and Dack[5] attacked the conclusion that sulfanilamide acted by toxin neutralization; while Osgood and Brownlee[6] admitted that they were not able to demonstrate toxin neutralization with ordinary methods, they expressed the belief that conditions in tissue cultures are more comparable to conditions in the body than is true of the other in vitro tests.

The basis for criticism by Hemmens and Dack was the fact that bacteriostasis, as a factor in reducing toxin formation, had not been properly evaluated. Osgood failed to record the size of the colonies showing smaller hemolytic zones in plates containing sulfanilamide. His data on cell suspensions could not be used to support his conclusion, since these were not in any sense quantitative.

Gross, Cooper and Lewis[7] reported that, in the presence of serum, sulfanilamide failed to neutralize streptococcus hemolysin. Huntington[8] reported that he was unable to neutralize hemolysin, fibrinolysin or scarlatinal toxin with sulfanilamide. Long, Bliss and Feinstone[9] found that sulfanilamide failed to protect guinea pigs and mice inoculated with lethal doses of botulinus toxin. They noted also that high concentrations of the drug in the blood of human beings did not alter positive reactions to the Dick test. Kemp[10] tested the neutralizing power of sulfanilamide for hemolysin, fibrinolysin and dermotoxin with negative results. In discussing his observations, Kemp states: "But there is something in these observations of more importance than this disagreement [with Osgood], and that is: whatever the action of sulfanilamide, the in vitro methods fail to reveal it . . ." He was probably led to this conclusion as a result of his failure to demonstrate an antihemolytic effect of sulfanilamide on blood agar plates. It is not clear why the excellent work of English and American investigators showing beyond reasonable doubt that the drug possesses powerful antibacterial properties in vitro was not considered by Kemp. His methods are not described in sufficient detail to enable one to decide why he failed to observe an antihemolytic effect secondary to bacteriostasis. It is not stated whether he observed a bacteriostatic effect.

It is now realized that several factors may prevent any considerable bacteriostatic effect of the drug. For instance, the size of the inoculum is important, as shown by Colebrook, Buttle and O'Meara,[3] who found that in the presence of very large numbers of organisms the drug was practically without effect. As Garrod[11] and Hoare[12] point out, this factor may account for Domagk's conclusion that there is little correlation between the in vivo and the in vitro effect of sulfanilamide.

Another factor that may have influenced Kemp's results is the type of strains used. Hoare[12] found nineteen of twenty-one strains of human origin responsive to sulfanilamide in vitro. The other two strains were from cases which did not respond to the drug. Also Bliss and Long[13] and Bliss, Long and Feinstone[14] felt that there was a significant correlation between in vivo and in vitro response. Since half of Kemp's

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1. Bliss, Eleanor A., and Long, P. H.: Observations on the Mode of Action of Sulfanilamide, J. A. M. A. **109:** 1524-1527 (Nov. 6) 1937.

2. Gay, F. P., and Clark, Ada R.: On the Mode of Action of Sulfanilamide in Experimental Streptococcus Empyema, J. Exper. Med. **66:** 535-547 (Nov.) 1937.

3. Colebrook, Leonard; Buttle, G. A. H., and O'Meara, R. A. Q.: The Mode of Action of *p*-Aminobenzenesulfonamide and Prontosil in Hemolytic Streptococcal Infections, Lancet **2:** 1323-1326 (Dec. 5) 1936.

4. Osgood, E. E., and Brownlee, Inez E.: Culture of Human Marrow: Studies on the Mode of Action of Sulfanilamide, J. A. M. A. **110:** 349-356 (Jan. 29) 1938.

5. Hemmens, Elizabeth S., and Dack, G. M.: Mode of Action of Sulfanilamide, J. A. M. A. **110:** 1209-1210 (April 9) 1938.

6. Osgood, E. E., and Brownlee, Inez E.: The Mode of Action of Sulfanilamide, J. A. M. A. **110:** 1770 (May 21) 1938.

7. Gross, Paul; Cooper, F. B., and Lewis, Marion: Inhibition of Streptococcal Hemolysin by Sulfonamide Compounds, Proc. Soc. Exper. Biol. & Med. **38:** 275-279 (March) 1938.

8. Huntington, R. W., Jr.: Failure of Sulfanilamide to Prevent Hemolysis, Fibrinolysis and Production of Erythrogenic Toxin by Hemolytic Streptococci in Vitro, Proc. Soc. Exper. Biol. & Med. **38:** 328-331 (April) 1938.

9. Long, P. H.; Bliss, Eleanor A., and Feinstone, W. H.: Mode of Action, Clinical Use and Toxic Manifestations of Sulfanilamide, J. A. M. A. **112:** 115-121 (Jan. 14) 1939.

10. Kemp, H. A.: On the Action of Sulfanilamide: Failure to Demonstrate Antihemolytic, Antifibrinolytic and Antitoxic Effect of the Drug, Texas State J. Med. **34:** 208-211 (July) 1938.

11. Garrod, L. P.: The Chemotherapy of Bacterial Infections, Lancet **1:** 1125-1129 (May 14), 1178-1182 (May 21) 1938.

12. Hoare, E. D.: Bactericidal Changes Induced in Human Blood and Serum by Sulfamidochrysoidine and Sulfanilamide, Lancet **1:** 655-659 (March 19) 1938.

13. Bliss, Eleanor A., and Long, P. H.: The Failure of Para-Aminobenzenesulfonamide Therapy in Urinary Tract Infections Due to Group D (Lancefield) Beta Hemolytic Streptococci, New England J. Med. **217:** 18-21 (July 1) 1937.

14. Bliss, Eleanor A.; Long, P. H., and Feinstone, W. H.: The Differentiation of Streptococci and Its Relation to Sulfanilamide Therapy, South. M. J. **31:** 303-308 (March) 1938.

strains were from cases which showed good clinical response, it seems unlikely that this factor explains his results.

A further factor of importance has been emphasized by Lockwood,[15] who finds that peptones interfere with the antibacterial power of sulfanilamide in vitro. Thus the composition of the culture medium must be taken into account.

Kemp's methods of measurement are not described. Hence, it is not clear whether these are sufficiently refined to detect slight differences in the size of the colony and the hemolytic zone in experimental and control sets.

As will be shown later, it is possible, when using a suitable medium and suitable quantitative methods, to demonstrate the bacteriostatic property of sulfanilamide in dilutions as high as 1:1,000,000 even when the medium contains as many as 150,000 colonies per cubic centimeter. With fewer colonies bacteriostasis is more pronounced.

Osgood[16] seems reluctant to grant any importance to the bacteriostatic effect of sulfanilamide as a mechanism whereby toxin formation is reduced. This is especially difficult to understand in view of his own clear demonstration of the antibacterial power of sulfanilamide in vitro. This property of the drug is well shown in his table 2.[4] Moreover, he noted and measured the smaller areas of hemolysis around colonies of beta streptococci grown in the presence of three different concentrations of the drug. He recorded regular and significant decreases in the diameter of the hemolytic zones. These observations he interpreted as evidence of toxin neutralization without recording the diameter of the colonies. It is obviously impossible to arrive at any conclusion as to the cause of the observed reduction in hemolysis without considering the bacteriostatic effect of the drug.

The question of decreased toxin production secondary to the decrease in the number of organisms is one of fundamental importance. This is the question raised in the criticism of Hemmens and Dack.[5] In their reply, Osgood and Brownlee[6] state: "The word 'neutralization' was poorly chosen and . . . we should have said 'The major action of sulfanilamide appears to be on the production of toxins or aggressins. We do not know to what this is due.'" In a later paper Osgood[17] states that "sulfanilamide's major action is prevention of formation of, or neutralization of, toxins." Here it is not clear what he means by "prevention of formation." He seems to imply inhibition of toxin formation out of proportion to inhibition of bacterial growth. In the same issue, in discussing Kemp's paper,[10] Osgood states: "The major action of sulfanilamide appears to be on the toxins or aggressins. We do not as yet know whether this is due to destruction of some substance necessary for the formation of these toxins or aggressins, to a direct action on the organism preventing the formation of toxins or aggressins, to the destruction of the nascent toxins or aggressins, to destruction of toxins or aggressins after they are formed, to catalysis of an antitoxin-toxin reaction or to a sufficiently slow rate of production of toxins or aggressins so that they are destroyed by the natural processes of oxidation as rapidly as they are formed."

15. Lockwood, J. S.: Studies on Mechanism of Action of Sulfanilamide; Effect of Sulfanilamide in Serum and Blood on Hemolytic Streptococci in Vitro, J. Immunol. **35:** 155-193 (Sept.) 1938.
16. Osgood and Brownlee (footnotes 4 and 6).
17. Osgood, E. E.: Culture of Human Marrow, Texas State J. Med. **34:** 206-208 (July) 1938.

In an effort to resolve this detailed and somewhat speculative list of possibilities into a smaller number of general propositions which can be tested experimentally, we list three obvious possibilities involved in the relation between bacteriostasis and inhibition of hemolysis (hemolysin being the only toxin considered in this paper). Decreased hemolysis in the presence of sulfanilamide might be (*a*) secondary to bacteriostasis caused by the drug, as demanded by the bacteriostatic theory (*b*) caused by neutralization of toxin, i. e., inactivation or destruction of toxin, or (*c*) due to "prevention of formation" of toxin, i. e., a reduction of toxin in excess of what might reasonably be regarded as secondary to the smaller number of organisms resulting from the bacteriostatic effect of the drug.

By the use of ordinary methods, it has now been established beyond reasonable doubt that sulfanilamide does not neutralize toxin. The latest paper on this phase of the problem is by Osgood and Powell.[18] They confirm the results of other investigators on this point. They do not, however, discuss the bearing of their observations on Osgood's previously published opinions on toxin neutralization, or the bearing of either on the bacteriostatic theory which demands reduced toxin formation as a consequence of bacteriostasis. In discussing this paper, it was stated in THE JOURNAL[19] that "The results of these experiments, therefore, fail to support, although they do not disprove, the earlier experiments with cultures of human bone marrow reported by the senior author."

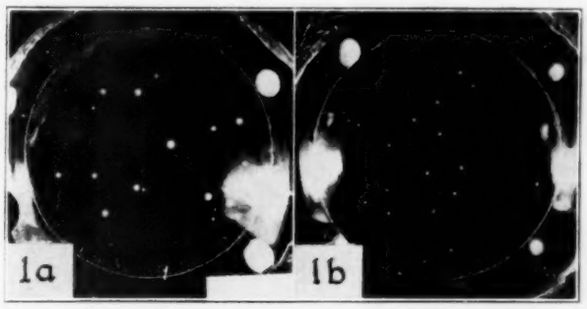

Fig. 1.—Control (*a*) and experimental cultures (*b*). Sulfanilamide 1:1,000; ninety-six hours; approximately 125 colonies per cubic centimeter; strain 2; no erythroctes in clot. Direct photograph, × 1½.

Evidence is offered later to show that, in tissue culture mediums composed chiefly of rabbit plasma and serum, sulfanilamide exerts a bacteriostatic effect on the three strains of beta hemolytic streptococci studied; that the effect varies directly with the concentration of the drug and inversely with the number of bacteria present; that a decrease in hemolysis is observed when bacteriostasis is observed; that the extent of the decrease of hemolysis does not suggest either toxin neutralization or "prevention of formation" of toxin beyond what might reasonably be expected as a result of the observed bacteriostasis, and that the drug inhibits the development of diffuse peripheries around colonies of beta streptococci.

MATERIALS AND METHODS

The routine tissue culture methods used have been described previously by King.[20] The method as applied

18. Osgood, E. E., and Powell, H. M.: Failure of Sulfanilamide to Inactivate Preformed Hemotoxins, Diphtheric Toxin or Tetanal Toxin, Proc. Soc. Exper. Biol. & Med. **39:** 37-40 (Oct.) 1938.
19. Sulfanilamide and Bacteriostasis, current comment, J. A. M. A. **111:** 2306 (Dec. 17) 1938.
20. King, J. T.: Tissue Culture Technic, Arch. f. exper. Zellforsch. **9:** 341-349 (No. 3) 1930; An "Activated" Extract for Coagulating Heparin-Plasma, ibid. **10:** 467-473 (No. 4) 1931.

to the study of neoprontosil has been described by King, Henschel and Green.[21]

The Maximow technic is used, the culture being planted on a 22 mm. round cover slip. This slip is fastened to a large cover (with saline solution), which is then inverted over a deep hollow ground slide and sealed with petrolatum and afterward with a petrolatum-paraffin mixture. Cultures are incubated as lying-drop preparations at 37.5 C. in a special down-draft incubator previously described by King.[22] Under these conditions there is no vapor in the dome of the chamber even in the early hours of incubation. The culture is composed of one drop of heparinized rabbit plasma and two drops of tissue extract made by extracting six day

TABLE 1.—*Effect of Varying the Number of Organisms on the Bacteriostatic Effect of Sulfanilamide 1: 1,000; Twenty-Four Hours; Strain 2*

Dilution of Bacterial Culture	Average Colony Diameter, Control	Average Colony Diameter, Experiment	Inhibition, per Cent
1:100,000	7.09	5.12	27.8
1:1,000,000	24.29	11.40	53.1
1:10,000,000	49.01	12.40	74.7

chick embryos with rabbit serum. The properties of this extract have been previously described by King and Henschel.[23]

When hemolysin is to be studied, sufficient rabbit erythrocytes are introduced to make a 5 per cent suspension in the final clot. Sulfanilamide is dissolved in 0.9 per cent saline solution and sterilized by filtration. A sufficient amount of this solution is added to the tissue extract to give the required concentration in the final medium. A corresponding amount of saline solution is added to the control medium.

Organisms are added to the tissue extract after suitable dilution of the original culture in Tyrode's solution to give the required concentration in the final medium.

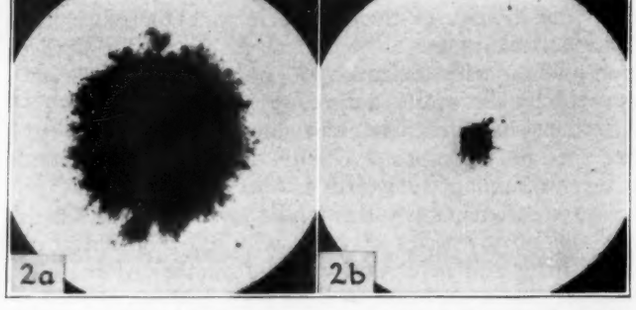

Fig. 2.—Control (*a*) and experimental (*b*) colonies. Sulfanilamide 1: 1,000, ninety-six hours; from 5 to 10 colonies per cubic centimeter; strain 2; no erythrocytes in clot. Slightly reduced from a photomicrograph with a magnification of 37 diameters.

The streptococci are grown in veal infusion broth. Cultures are approximately 18 hours old when used.

The three strains of beta streptococci used are all of human origin. These strains are mouse virulent. The strain BG was isolated from the cerebrospinal fluid of a patient with meningitis. The clinical response to sulfanilamide was prompt. Strain 2 was isolated from the blood in a fatal case of septicemia. Strain 40, Lancefield group C, was isolated from a culture taken on material from the throat.

Colony diameter is used as an index of the bacteriostatic effect of the drug. The diameter of the hemolytic zone is used as an index of the hemolytic activity of the colony. The term "hemolytic index" is used to describe the amount of hemolysis in relation to the size of the colony; i. e., the diameter of the zone of hemolysis divided by the diameter of the colony.

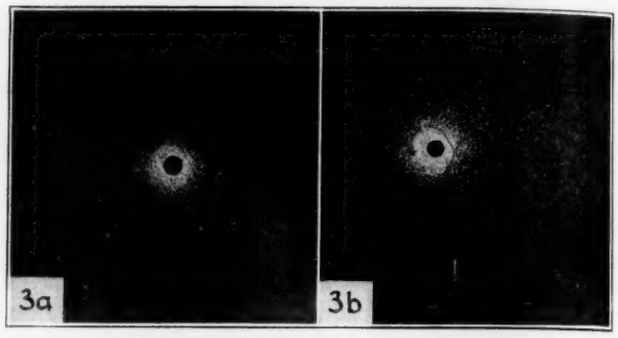

Fig. 3.—Control (*a*) and experimental (*b*) colonies. Sulfanilamide 1: 1,000; twelve hours; strain 2; 5 per cent erythrocytes in clot. Slightly reduced from a photomicrograph with a magnification of 37 diameters.

Measurements are made at a magnification of 60 diameters, with a standardized ocular micrometer (114 units = 1 mm.). With a mechanical stage, accurate measurements can be made of the diameter of the colony and zone of hemolysis.

Photomicrographs are made on process film. Exposure is kept down to the minimum required to register the lysed area adjacent to the colony. In this manner maximal contrast is obtained between lysed and unlysed portions of the clot. Films are developed for strong contrast. Direct photographs of cultures containing no erythrocytes are taken against a black background on process film. Panchromatic process film is used for cultures containing erythrocytes.

RESULTS

Streptococci grow rapidly in this medium, colonies usually becoming visible between the fourth and the sixth hour when the medium contains no erythrocytes. Although some strains are fibrinolytic, those used in this study showed no lysis of the clot. The usual inverse relationship between the number of colonies and the size of the colonies is observed.

TABLE 2.—*Bacteriostatic Effect of Sulfanilamide 1: 1,000; at Twenty-Four Hours; Strain BG; 150,000 Colonies per Cubic Centimeter*

Sulfanilamide Concentration	Colony Diameter	Inhibition, per Cent
Controls	5.67	....
1:1,000	4.52	20.3
1:10,000	4.67	17.6
1:100,000	4.81	15.2
1:1,000,000	4.92	13.2

The time at which colonies attain maximal size depends on the number of colonies present. When the medium contains 150,000 colonies or more per cubic centimeter, growth is essentially complete in twelve hours. When the colony count per cubic centimeter is 10 or less, growth continues for at least five days.

21. King, J. T.; Henschel, A. F., and Green, Beryl S.: Influence of Prontosil Soluble on Beta Hemolytic Streptococci Growing in Tissue Culture Media, Proc. Soc. Exper. Biol. & Med. **38**: 810-812 (June) 1938.
22. King, J. T.: Special Incubator for Tissue Cultures, Arch. f. exper. Zellforsch. **20**: 208-212 (No. 2) 1937.
23. King, J. T., and Henschel, A. F.: Comparison of Serum and Saline Extracts as Nutritive Media for Mammalian Lymph Node Cultures, Proc. Soc. Exper. Biol. & Med. **32**: 1224-1226 (May) 1935.

The inhibition caused by a given concentration of sulfanilamide varies inversely with the number of colonies present. Table 1 shows the result of three dilutions of a culture of strain 2 in the medium without erythrocytes.

Figure 1 shows the effect of sulfanilamide with approximately 125 colonies per cubic centimeter and figure 2 with from 5 to 10 colonies per cubic centimeter.

With a constant number of bacterial colonies the inhibitory influence of the drug varies directly with the concentration. Table 2 shows the bacteriostatic effect on strain BG when a heavy inoculum is used.

TABLE 3.—*Effect of Sulfanilamide 1:1,000 on Colony Size and Hemolysis; Strain 2*

	Controls			Sulfanilamide				
Time	Diameter of Colony	Diameter of Hemolytic Zone	Hemolytic Index	Diameter of Colony	Diameter of Hemolytic Zone	Hemolytic Index	Colony Inhibition, per Cent	Inhibition of Hemolysis, per Cent
18 hrs.	39.8	65.0	1.63	12.4	32.4	2.62	68.8	50.1
24 hrs.	78.5	132.9	1.69	13.7	57.4	4.17	82.4	56.8
48 hrs.	214.7	354.0	1.64	33.7	208.1	6.20	84.3	41.2
3 days	252.4	399.5	1.58	43.2	245.7	5.69	82.9	38.5

The data in table 2 are based on measurement of between 225 and 300 colonies (in three cultures) in each concentration of sulfanilamide and control set (three cultures). With this number of colonies, strain BG shows little, if any, qualitative difference between experimental and control colonies.

In strong contrast to the very moderate inhibition shown in table 2 in the presence of a large number of colonies, this strain regularly shows more than 80 per cent inhibition with 25 colonies or less per cubic centimeter (sulfanilamide 1:1,000).

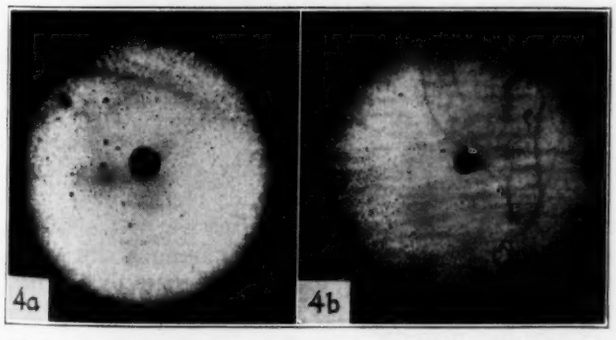

Fig. 4.—Control (*a*) and experimental (*b*) colonies. Sulfanilamide 1:1,000; forty hours; strain 2; 5 per cent erythrocytes in clot. Slightly reduced from a photomicrograph with a magnification of 37 diameters.

TOXIN NEUTRALIZATION

When 5 per cent rabbit erythrocytes are added to the medium before clotting takes place, it is possible to determine the size of the colony at the time at which hemolysis becomes evident. Subsequent measurements of the diameter of the colony and of the zone of hemolysis make possible a correlation between these two factors.

Early observations and measurements show that, when a colony attains a given size, hemolysis commences whether sulfanilamide is present or not. Hemolysis starts when the colony attains a size of approximately 10 units.

Figure 3 shows a twelve hour control and experimental colonies of approximately the same size. There is no evidence that a high concentration (100 mg. per hundred cubic centimeters) of sulfanilamide has reduced the hemolytic activity of the colony. As is evident from tables 3 and 4, there is a lag in the development of experimental colonies due to the bacteriostatic effect of the drug. This results in less hemolysis in

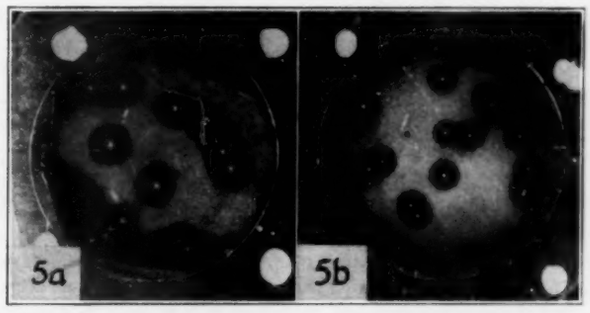

Fig. 5.—Control (*a*) and experimental (*b*) cultures. Sulfanilamide 1:1,000; twenty-four hours; strain 2; 5 per cent erythrocytes in clot. Direct photograph, × 1½.

experimental cultures at a given time. However, when experimental colonies are compared with control colonies of the same size, there is no evidence of hemolysin neutralization.

Study of the subsequent development of the cultures likewise fails to reveal any evidence of neutralization of preformed hemolysin. Figure 4 shows well developed colonies from experimental and control sets (forty hours).

Figure 5 is made from direct photographs of experimental and control cultures of strain 2 (sulfanilamide 1:1,000). In this figure the lysed areas are dark while the unlysed portion of the clot is light.

Detailed observations on two experiments with strain 2 are shown in tables 3 and 4. In the experiment shown in table 3 the control colonies showed the usual diffuse peripheries. In the other experiment (table 4) the control colonies grew as compact masses.

In both experiments typical inhibition of both colony and hemolytic zone is shown.

TABLE 4.—*Effect of Sulfanilamide 1:1,000 on Colony Size and Hemolysis; Strain 2*

	Controls			Sulfanilamide				
Time	Diameter of Colony	Diameter of Hemolytic Zone	Hemolytic Index	Diameter of Colony	Diameter of Hemolytic Zone	Hemolytic Index	Colony Inhibition, per Cent	Inhibition of Hemolysis, per Cent
9 hrs.	10	..	....	5	..	....	50.0	....
11 hrs.	13	25	1.92	6	..	....	53.9	....
14 hrs.	38	91	2.39	11	32	2.91	71.1	64.8
22 hrs.	57	232	4.07	21	82	3.90	63.2	64.7
24 hrs.	59	264	4.47	27	110	4.07	54.2	58.3
35 hrs.	67	316	4.72	41	215	5.24	38.8	32.0
44 hrs.	76	327	4.30	49	266	5.43	35.5	18.7
2½ days	81	352	4.35	60	300	5.00	25.9	14.8

In all cases it has been noted that the hemolytic index rises to a maximum and then declines somewhat. The experimental cultures reach the maximum later than the controls.

The hemolytic index is higher in the cultures containing sulfanilamide than in the controls. As will be noted later, the significance of this fact is not entirely clear at present.

BACTERICIDAL PROPERTIES OF SULFANILAMIDE

In this medium there has been no consistent reduction in the number of colonies in experimental cultures.

QUALITATIVE CHANGES CAUSED BY SULFANILAMIDE

With large inoculums no characteristic change is noted. Sometimes experimental colonies appear less dense. When the inoculum is sufficiently small to permit colonies to attain any considerable size, the drug causes qualitative change in those strains which show diffuse peripheries. The drug regularly inhibits the development of such peripheries. The resulting colonies are small and compact. The strains studied have not shown a characteristic qualitative response to the drug when they failed to develop diffuse peripheries.

It has been noted that colonies whose diffuse peripheries have been inhibited by sulfanilamide frequently show heavy chains invading the clot. The amount of chain formation is quite variable. In our experience, from three to twelve chains can be regarded as typical. When chains are present they are not evenly distributed around the colony but are grouped in a loose net in a rather limited area.

Rarely a colony may develop a complete periphery composed of this typical loose network of heavy chains. We have seen only a few such colonies and those developed rather late.

We wish especially to emphasize the difference between this type of periphery and the normal, diffuse periphery seen around control colonies. In the latter the organisms are widely scattered, singly and in groups of two or three. In the presence of sulfanilamide, however, the normal mechanism of division is so modified as to produce long chains.

Gay and Clark [2] had observed earlier that when streptococci were grown in serum containing sulfanilamide the organisms grew in long chains of pleomorphic and metachromatic forms. Later, Meyer [24] described "great masses of markedly deformed, swollen streptococci, growing in endless chains," in relation to the "clumping reaction," which he observed in serum-broth cultures of streptococci containing a sulfanilamide-sugar compound.

Lockwood [15] described long chains of abnormal streptococci growing in mediums containing sulfanilamide. This tendency to form long chains in the presence of the drug was also noted by Chandler and Janeway.[25]

COMMENT

Of the many factors having a probable bearing on the mechanism of action of sulfanilamide, we are concerned in this paper with the following: (1) the bacteriostatic action in vitro as influenced by the concentration of the drug and the size of the inoculum; (2) the correlation between the bacteriostatic effect and the amount of hemolysis; (3) the qualitative changes caused by the drug.

It is now realized that certain experimental conditions are required to demonstrate the effects of sulfanilamide in vitro, and all failures to demonstrate such effects when therapeutically responsive strains of beta streptococci are used must be examined in the light of this knowledge.

Colebrook, Buttle and O'Meara [3] reported that the drug was almost without effect in the presence of very large numbers of organisms. Lockwood [15] also found a greater effect when using a smaller inoculum. Recently, Chandler and Janeway [25] reported the same experience. These investigators worked with fluid mediums.

In tissue culture clots we have found the bacteriostatic effect of the drug to vary inversely with the number of colonies present (table 1). That it is possible, however, to demonstrate moderate bacteriostasis in this medium, even in the presence of relatively large numbers of organisms, is shown in table 2.

Lockwood [15] found that peptones interfere with the action of sulfanilamide and pointed out the importance of avoiding the use of mediums containing such substances if one wished to obtain the full effect of the drug.

Lockwood, Coburn and Stokinger [26] reported, on the basis of clinical experience, that "the presence of débris, human or bacterial, diminished the effectiveness of sulfanilamide on the hemolytic streptococcus. In each instance the organisms remaining in broken down tissue maintained their virulence. It is not known whether the débris itself had a protective action on the organisms or whether there was insufficient penetration of the drug into the locus."

We [27] have found that the presence of a small fragment of tissue in a tissue culture greatly antagonizes the effects of sulfanilamide even at a considerable distance from the fragment. We have observed this effect with concentrations of sulfanilamide as high as 140 mg. per hundred cubic centimeters. We believe that the products of tissue disintegration exercise a protective effect on the organisms.

Since the extracts used in making the clots of tissue culture were made by shaking six day chick embryos in serum, the question might be raised whether enough peptone-like substance would be extracted to cause a "peptone effect"; i. e., a reduction in the effect of sulfanilamide.

It was pointed out by Colebrook, Buttle and O'Meara [3] that the effect of sulfanilamide was much less marked in the blood of the small laboratory animals than in human blood. Except for very small inoculums, they found the drug to be bacteriostatic but not bactericidal in the blood of these animals. Gay and Clark [2] observed only bacteriostasis in rabbit serum containing the drug. In neither of these cases was there any addition of peptone-like substance. In view of these facts and of the further fact, already noted, that the drug is much more effective in the cell-free medium than in the medium containing a small tissue fragment, we assume tentatively that the medium reacts as though free of any significant amount of peptone-like material.

As pointed out earlier, Bliss and Long [13] and Bliss, Long and Feinstone [14] obtained satisfactory correlation between in vivo and in vitro response, and Hoare [12] found 100 per cent correlation in a study of twenty-one strains.

In the present study we have used only Lancefield group A and C strains. The strains reported, and others less intensively studied, proved responsive to the drug in the tissue culture medium.

It now seems safe to assume that all therapeutically responsive strains of beta hemolytic streptococci are inhibited by sulfanilamide in vitro if the experimental conditions are suitable.

24. Meyer, Fritz: New Studies in Sulfanilamide Therapy, Quart. Bull. Sea View Hosp. **3**: 380-404 (July) 1938.

25. Chandler, C. A., and Janeway, C. A.: Observation on the Mode of Action of Sulfanilamide in Vitro, Proc. Soc. Exper. Biol. & Med. **40**: 179-184 (Feb.) 1939.

26. Lockwood, J. S.; Coburn, A. F., and Stokinger, H. E.: Studies on the Mechanism of Action of Sulfanilamide, J. A. M. A. **111**: 2259-2264 (Dec. 17) 1938.

27. King, J. T., and Henschel, A. F., to be published.

In view of the well known ability of the streptococcus to produce destructive toxins, it is natural that considerable interest has attached to the possibility that sulfanilamide might either reduce the amount of toxin formed or neutralize toxin. The bacteriostatic theory assumes that there is a reduction in the amount of toxin formed secondary to the reduction in the number of organisms brought about by the drug. In the tissue culture medium we have always found that when the drug causes a decrease in the size of the colony it also causes a decrease in the size of the hemolytic zone. Typical results are shown in tables 3 and 4.

We have observed that hemolysis starts when the colony reaches a certain size whether or not sulfanilamide is present. There is a lag in the development of experimental colonies as compared with the controls. Otherwise the sequence of events is fundamentally alike in the two. Study of the subsequent development of the colony shows that the drug continues to exert a bacteriostatic effect and that the amount of hemolysis is less in experimental cultures. On the basis of colony size, however, colonies growing in 100 mg. per hundred cubic centimeters of the drug produce a larger rather than a smaller zone of hemolysis; i. e., they show a higher hemolytic index. Possible explanations for the higher hemolytic index observed in experimental cultures will be considered after the qualitative changes caused by the drug have been discussed.

It is clear that if the drug neutralized hemolysin or reduced the formation of hemolysin out of proportion to the reduction in the number of organisms, the hemolytic index of experimental colonies would be lower. This is not the case, however. Consequently, we can only conclude that such reduction in hemolysis as is observed is secondary to the bacteriostatic effect of the drug.

Most of the strains available to us grow with diffuse peripheries in this medium, provided the inoculum is not too large. Some strains, for example strain 2, are not constant in this regard, at times showing peripheries and at other times growing as compact colonies.

We have never seen a normal diffuse periphery in a culture containing sulfanilamide unless the effects of the drug were antagonized by the presence of tissue.[27] The drug inhibits the rapid invasion of the clot usually seen around control colonies.

As already noted, an inhibited colony may show a variable number of long, heavy chains projecting from some point on the periphery or, rarely, a complete periphery composed of a loose network of such chains.

In considering possible explanations for the higher hemolytic index observed for colonies growing in cultures containing sulfanilamide, the qualitative change in colony form usually caused by the drug must be taken into account. It has been pointed out that the drug inhibits the development of the wide, diffuse periphery usually seen around colonies of beta streptococci in this medium. As may be seen by comparing the control colonies shown in tables 3 and 4, this diffuse periphery is not as active in producing hemolysis as the more dense central part of the colony. In the experiment detailed in table 3, strain 2 grew with the usual peripheries. The hemolytic index reached a maximum of 1.69. An experiment with the same strain is shown in table 4, in which the colonies are of the compact type showing a maximum hemolytic index of 4.72. From these facts it is evident that a more compact colony has a higher hemolytic index.

It is possible that the higher hemolytic index observed in cultures containing sulfanilamide is due to the formation of a more compact colony. It is clear that this factor is important when the controls grow with the usual diffuse peripheries, as in the experiment shown in table 3. The interpretation is complicated however by the fact that, even when the control colonies fail to develop diffuse peripheries, sulfanilamide causes a higher hemolytic index. In this case it is not evident that the drug causes the development of more compact colonies, but the possibility cannot be ruled out.

We have considered the possibility that erythrocytes might be more vulnerable to lysis by streptococcus hemolysin in the presence of sulfanilamide. There is, however, no experimental evidence to support this theoretical possibility.

Another possible explanation is based on the fact that sulfanilamide is known to form numerous conjugation products. Czarnetsky and his associates[28] have found that certain derivatives of the streptococcus will conjugate with the drug to form hemolytic products. It is therefore possible that the drug combines with some product of bacterial metabolism to form a hemolytic agent. Should this ultimately prove to be true, it is interesting to speculate what bearing it might have on the cause of the severe anemias now known to occur occasionally during administration of the drug.

SUMMARY

A tissue culture study has been made of the bacteriostatic and antihemolytic properties of sulfanilamide.

All strains of beta streptococci studied were inhibited.

The bacteriostatic effect varied directly with the concentration of the drug and inversely with the number of bacterial colonies.

Reduction in hemolysis was observed to accompany bacteriostasis.

Correlation of the reduction in hemolysis with the observed bacteriostasis leads to the conclusion that the antihemolytic effect is secondary to bacteriostasis.

The drug regularly inhibits the wide, diffuse peripheries usually seen around colonies of beta streptococci growing in clots of tissue culture.

The drug causes the development of abnormal, long chains of streptococci.

CONCLUSIONS

Sulfanilamide is bacteriostatic for the strains of beta streptococci studied. The effect varies directly with the concentration of the drug and inversely with the number of bacteria.

The antihemolytic effect is secondary to the bacteriostatic effect. There is no evidence that the drug neutralizes hemolysin or reduces its formation beyond what can be accounted for on the basis of the reduced number of organisms involved.

The drug modifies the normal mode of division and reduces the ability of the organisms to invade the clot.

28. Czarnetsky, E. J., and Calkins, H. F.: Some Reactions of Sulfanilamide with Nucleoproteins and a Suggested Mechanism of Action of Sulfanilamide, J. Bact. **36:** 330 (Sept.) 1938.

Life History of the Housefly.—The housefly passes through a complex metamorphosis, i. e. egg, larva (maggot), pupa and adult or fully winged insect. Under warm summer temperatures the egg stage requires about twenty hours, the larval stage about five days, the pupa about four days, a total of about ten days from egg to adult insect. This allows for the development of from ten to twelve generations in one summer.—Herms, William B.: Medical Entomology, New York, Macmillan Company, 1939.

EXPERIMENTAL CHEMOTHERAPY WITH SULFANILAMIDE AND RELATED COMPOUNDS

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Bacterial chemotherapy has emerged from the laboratory. It is primarily in the laboratory that progress must be made in the development of more effective compounds and of compounds active against diseases as yet not influenced by chemical treatment. It is also in the laboratory that a better understanding of the mode of action of these drugs and of their toxic effects can be obtained.

I wish to discuss some aspects of the problem from a laboratory point of view. This new field has been characterized by too hasty clinical application of experimental results. Some shortcomings in our knowledge and some of the difficulties encountered in transferring results from one species to another will be brought out. This paper is not intended to be a comprehensive review of the field of bacterial chemotherapy but a discussion of certain phases of the subject with which I have had experience in the laboratory.

PHARMACOLOGIC CONSIDERATIONS

The acute toxicity of sulfanilamide for several species of higher animals has been adequately established. Given in single doses by mouth, it is tolerated in amounts of from 1.5 to 3 Gm. per kilogram, depending on the species. The work of Marshall [1] and his colleagues has added much to an understanding of the acute toxicity, absorption, distribution in the body and excretion of sulfanilamide. It must be pointed out that these toxicity values were established on normal animals. My associates and I have observed that in mice rendered extremely ill by infection and toxins, such as is seen following the injection of large numbers of meningococci of low virulence to mice, deaths were often encountered following one third of the maximum dose normally tolerated.

Of more importance to the clinician is the question of chronic toxicity, and in this our knowledge is inadequate. Marshall, Emerson and Cutting [2] found sulfanilamide well tolerated over a period of weeks by the rat and dog. Molitor and Robinson [3] have quite recently studied the acute and chronic toxicity of sulfanilamide and benzysulfanilamide in mice, rats, dogs and rabbits. With large doses of sulfanilamide cumulative toxicity and pathologic changes were manifest. Their chronic toxicity studies on rabbits were unsatisfactory. Contrary to prevalent opinion, water increased the toxicity of sulfanilamide in their experience. We [4] have found that in the rabbit under certain dietary restrictions from 0.5 to 1 Gm. per kilogram for two weeks produced toxic symptoms and frequent deaths. Chickens on this dosage showed emaciation, motor weakness and a high mortality. Halpern and Mayer [5] and Rich [6] have also noted cumulative toxic effects in the guinea pig. Still another illustration of species variation in toxicity is seen in that frequent toxic manifestations observed in human beings such as fever, dermatitis and hematologic changes are encountered rarely or not at all in experimental animals. However, cyanosis has recently been produced in rats and chickens, and susceptible species may be found in which the other toxic effects seen in man may be produced.

In dealing with compounds of low water solubility this discrepancy between acute and chronic toxicity may be even more marked. Thus with sulfanilyl sulfanilamide the enormous single doses tolerated by animals give a misleading indication of the results obtained on repeated administration. It must therefore be concluded that the acute toxicity of this group of drugs is no reliable criterion of the effects to be obtained on their repeated administration and that considerable variation in toxic manifestations may be encountered from one species to another.

THERAPEUTIC RESULTS IN ANIMALS

There is a definite need for some standardization of the experimental assay of chemotherapeutic activity of these new drugs. Widely divergent results have been obtained in different laboratories. Apart from such factors as toxicity and the rate of absorption and excretion, therapeutic effectiveness is influenced by the dosage, the route of administration, the onset and duration of therapy, the period of observation following therapy, the strain of organism, the infecting dose and virulence of the organisms, the species and number of the animals and the condition of the animals employed.

While there is universal agreement on the activity of sulfanilamide in experimental beta hemolytic streptococcus infections, the dosage required to bring about the survival of the majority of infected mice varies from one third to one tenth of the maximum tolerated dose. At best this is not an impressive therapeutic index and emphasizes from the laboratory point of view the necessity for large doses to bring about good therapeutic results.

On pneumococcic infections in mice sulfanilamide has a less marked action, bringing about chiefly a prolongation of life.[7] That this degree of activity cannot be accepted as valid for man is shown by the fact that sulfanilamide has a much better action in pneumococcic infections in rabbits, and in rats a high percentage of cures can be effected.[8]

The increased effectiveness of sulfapyridine against pneumococcic infections was first demonstrated by Whitby.[9] While preliminary experiments have not

Read before the Section on Pathology and Physiology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 18, 1939.

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3. Molitor, Hans, and Robinson, Harry: Some Pharmacological and Toxicological Properties of Sulfanilamide and Benzylsulfanilamide, J. Pharmacol. & Exper. Therap. **65:** 405 (April) 1939.

4. Rosenthal, S. M.: Studies in Chemotherapy: VIII. Some Toxic Effects of Repeated Administration of Sulfanilamide and Sufanilyl Sulfanilamide ("Di-Sulfanilamide") to Rabbits and Chickens, Pub. Health Rep. **54:** 95 (Jan. 27) 1939.

5. Halpern, B. N., and Mayer, R. L.: Toxicité expérimentale comparée de quelque substances antistreptococciques, Presse méd. **45:** 747, 1937.

6. Rich, A. R., and Follis, R. H., Jr.: Inhibitory Effect of Sulfanilamide on the Development of Experimental Tuberculosis in the Guinea Pig, Bull. Johns Hopkins Hosp. **62:** 77 (Jan.) 1938.

7. Rosenthal, S. M.; Bauer, Hugo, and Branham, S. E.: Studies in Chemotherapy: IV. Comparative Studies of Sulfonamide Compounds in Experimental Pneumococcus, Streptococcus, and Meningococcus Infections, Pub. Health Rep. **52:** 662 (May 21) 1937. Cooper, F. B.; Gross, Paul, and Mellon, R. R.: Action of *p*-Aminobenzenesulfonamide on Type III Pneumococcus Infections in Mice, Proc. Soc. Exper. Biol. & Med. **36:** 148 (March) 1937.

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9. Whitby, L. E. H.: Chemotherapy of Bacterial Infections, Lancet **2:** 1095 (Nov. 12) 1938.

confirmed the uniformly high curative effects of this compound reported by him in mouse infections, results have shown a definite superiority over sulfanilamide.

The effectiveness of sulfanilamide in experimental meningococcic infections, demonstrated first by Buttle, Gray and Stephenson,[10] has been amply confirmed. It should be noted that the two infections most susceptible to therapy in the laboratory, streptococcic and meningococcic, have given the most encouraging results in the clinic.

On staphylococcic infections in mice sulfanilamide has only a slight activity, but more favorable effects have been obtained with sulfanilyl sulfanilamide,[11] and recently with sulfapyridine.[12]

Space will permit only brief mention of the positive laboratory results in other infections. Following the successful clinical use in gonorrhea, Levaditi[13] first demonstrated marked curative action of sulfanilamide and some related compounds in gonococcic "toxi-

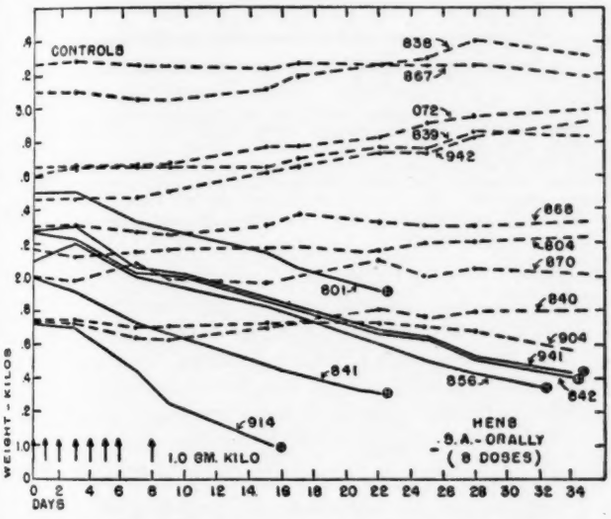

Chart 1.—Eight daily doses of 1 Gm. per kilogram of sulfanilamide to chickens caused progressive loss of weight, weakness, particularly marked in the legs, and delayed death.

infection" in mice. Levaditi[14] had also demonstrated for several bacterial endotoxins a true antitoxic action for some sulfur compounds, although no effect could be shown against bacterial exotoxins.

Favorable laboratory results have been reported in infection with Clostridium welchii,[15] Escherichia coli,[16] brucellosis,[17] Bacillus aertryke, B. typhosus[18] and B. pestis.[19] An inhibitory but not curative effect has been found in experimental tuberculosis in guinea pigs.[6] Against malaria some effect has been found in monkeys but none in bird malaria.[20] Dr. Wooley and I have recently confirmed our earlier results[21] of a slight protective action with Domagk's original prontosil against infections in mice with the virus of lymphocytic chorio-

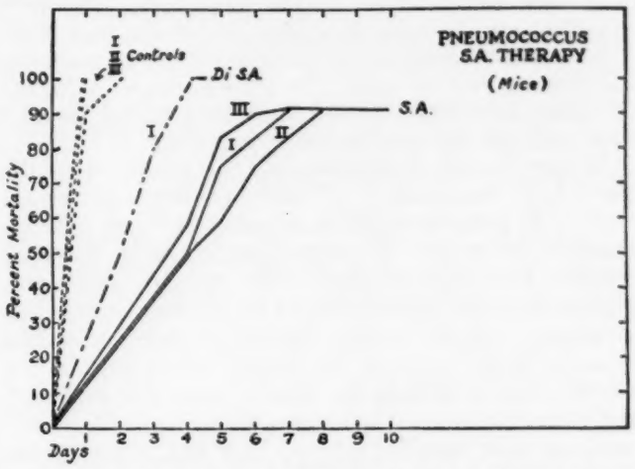

Chart 2.—Sulfanilamide and sulfanilyl sulfanilamide therapy of pneumococcic infections (Mulford strains types I, II and III) in mice. Sulfanilamide from 0.5 to 1 Gm. per kilogram given subcutaneously for from four to six days following intraperitoneal inoculation of organisms.

meningitis. Sulfanilamide was inactive. Among other virus diseases a definite curative action with sulfanilamide and some derivatives has been shown by Levaditi[22] for lymphogranuloma venereum. Suggestive results with some sulfanilamide derivatives in influenza virus infections in mice have been reported by Climenko, Crossley and Northey[23] and by Oakley.[24] On the virus

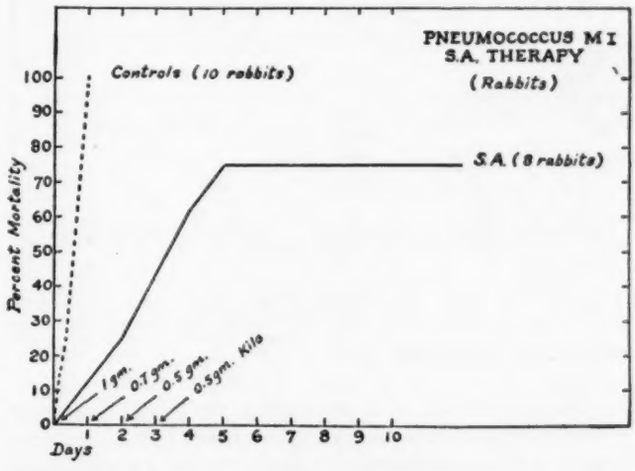

Chart 3.—Sulfanilamide therapy of type I pneumococcus in the rabbit. Infecting dose of organisms 1.5 cc of 10^{-4} intraperitoneally. Drug given subcutaneously as indicated.

of canine distemper conflicting results have been obtained since Dochez and Slanetz[25] first reported successes with sulfanilyl sulfanilate.

10. Buttle, G. A. H.; Gray, W. H., and Stephenson, Dora: Protection of Mice Against Streptococcal and Other Infections by *p*-Aminobenzenesulfonamide and Related Substances, Lancet **1:** 1286 (June 6) 1936.
11. Mellon, R. R.; Shinn, L. E., and McBroom, Josephine: Therapy of Experimental Staphylococcus Infections with Sulfonamide Compounds, Proc. Soc. Exper. Biol. & Med. **37:** 563 (Dec.) 1937.
12. Whitby.[9] Mayer.[16]
13. Levaditi, Constantin, and Vaisman, Aaron: La toxi-infection gonococcique expérimentale et son traitement chimiothérapique, Presse méd. **45:** 1371 (Sept. 29) 1937.
14. Levaditi, Constantin, and Vaisman, A.: Chimiothérapie antiendotoxique, Ann. Inst. Pasteur **61:** 635 (Dec.) 1938.
15. Long, P. H.; Bliss, Eleanor, and Feinstone, W. H.: Sulfanilamide, J. A. M. A. **112:** 115 (Jan. 14) 1939.
16. Mayer, R. L.: Activité de l'α (P. aminophényl-sulfamido)-pyridine dans les infections colibacillaire et staphylococcique de la souris, Compt. rend. Soc. de biol. **129:** 480, 1938.
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19. Schütze, Harry: Chemotherapy in Plague Infection, Lancet **1:** 266 (Feb. 4) 1939.
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21. Rosenthal, S. M.; Wooley, J. G., and Bauer, Hugo: Studies in Chemotherapy: VI. The Chemotherapy of Choriomeningitis Virus Infection in Mice with Sulfonamide Compounds, Pub. Health Rep. **53:** 1211 (Sept. 3) 1937.
22. Levaditi, Constantin: Chimiothérapie de la lymphogranulomatose inguinale expérimentale, Compt. rend. Soc. de biol. **128:** 138, 1938.
23. Climenko, D. R.; Crossley, M. L., and Northey, E. H.: The Protective Action of Certain Sulfanilamide Derivatives in Experimental Influenza Infections, J. A. M. A. **110:** 2099 (June 18) 1938.
24. Oakley, C. L.: Chemotherapy of Virus Infections, Brit. M. J. **1:** 895 (April 23) 1938.
25. Dochez, A. R., and Slanetz, C. A.: The Treatment of Canine Distemper with a Chemotherapeutic Agent, Sodium Sulfanilyl Sulfate, Science **87:** 142 (Feb. 11) 1938.

COMBINED DRUG AND SERUM THERAPY

Although the opportunities previous to the discovery of prontosil for studying the relationship between drug therapy and therapy with specific serum have not been numerous, two earlier examples of a synergistic effect have been demonstrated in the laboratory. Moore [26] employed ethylhydrocuprine plus antiserum, and Neufeld [27] used "Aurodetoxin" plus antiserum in pneumococcic infections in mice. In both instances a higher curative effect was obtained with combination therapy than with the use of drug or serum alone.

In our limited investigations, the results with the use of a combination of sulfanilamide and serum therapy in pneumococcic, meningococcic [28] and streptococcic [29] infections in mice demonstrated in each instance a synergistic effect. The curative action was greater than the additive effects of the two agents used separately. Similar results for pneumococcic infections in mice were reported by Gross and Cooper,[8] for streptococcic infections by Meyer [30] and Loewenthal,[31] and for meningococcic infections by Brown.[32] Osgood,[33] working with in vitro cultures of bone marrow, has also reported augmented effects on pneumococci when both drug and specific antiserum were present.

These results are in harmony with the concept that the drug acts directly on the organisms, in some way

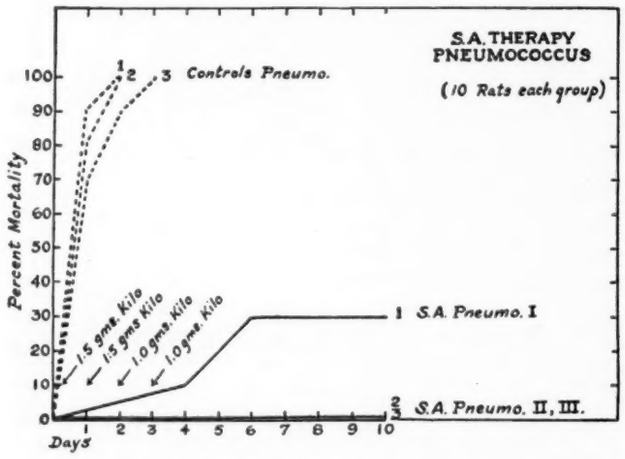

Chart 4.—The action of sulfanilamide in pneumococcic infections in rats. One cc. of broth culture of Mulford type I pneumococcus, diluted 10^{-5}; type II, 10^{-2}; type III, 10^{-4}, intraperitoneally. Drug given subcutaneously as indicated at arrows.

damaging or inhibiting them, so that the final eradication of the infection can be brought about by the natural defense mechanisms of the body.[34] In experimental infections it is difficult to bring about sterilization of the animal by brief periods of therapy, and under these circumstances a high percentage of relapses and late deaths occur. In the presence of severe infections this would emphasize the need for continued drug therapy, so that the defense forces of the body may be given

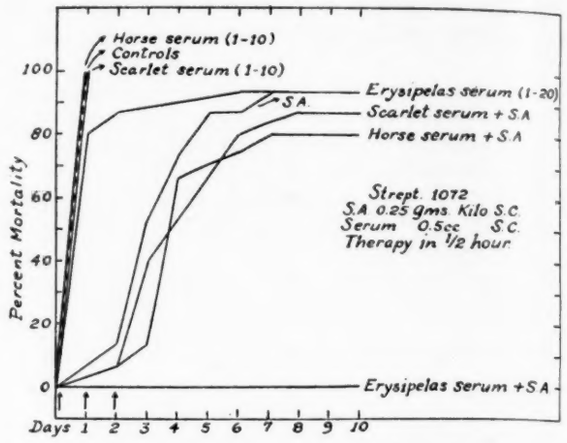

Chart 5.—The synergistic action of sulfanilamide and serum (antibacterial) therapy in experimental streptococcic septicemia in mice; ten mice to each group; dosage of serum and drug adjusted so that either alone had little curative action; combination therapy yielded a high percentage of cures; treatment given at times indicated by arrows; streptococcus originally isolated from a case of scarlet fever; similar results obtained with streptococci isolated from erysipelas and from general sepsis.

adequate opportunity to mobilize; when such forces are inadequate, experimental observations suggest the favorable effects of employing specific serum therapy, when such is available, in addition to drug therapy. While preliminary clinical use of combination therapy is suggestive, particularly in such conditions of high mortality as pneumococcic meningitis,[35] further laboratory and clinical experience is needed to evaluate this procedure.

THE RELATION OF CHEMICAL STRUCTURE TO CHEMOTHERAPEUTIC ACTION

Since the discovery of prontosil, an impressive number of compounds have been investigated for antibacterial action. Of the numerous derivatives of sulfanilamide few possess greater activity than the parent compound against streptococci, but sulfapyridine is one illustration that derivatives can be obtained with enhanced activity against specific infections. The discovery by Buttle [36] and Fourneau [37] that 4,4′-diamino diphenylsulfone and certain derivatives were many times as active against streptococci as sulfanilamide marked an important advance, since these compounds contain no sulfonamide group. The active radical common to this entire class of compounds may be characterized as

(after Fourneau [38]) N⬡S

Levaditi [39] has reported activity for dihydroxy diphenylsulfone, demonstrating that nitrogen is not in all cases necessary for activity.

26. Moore, H. F.: The Chemoserotherapy of Experimental Pneumococcal Infections, J. Exper. Med. **22:** 389, 1915. Boehncke, K. E.: München. med. Wchnschr. **60:** 398 (Feb. 25) 1913.

27. Neufeld, F., and Collier, W. A.: Chemo- und serotherapeutische Versuche bei der Pneumokokken-pneumonie der Maus, Ztschr. f. Hyg. u. Infektionskr. **117:** 129, 1935.

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34. Levaditi, Constantin: La chimiothérapie des infections microbiennes: son mécanisme d'action, Schweizer. Ztschr. f. allg. Path. u. Bakt. **1:** 365 (Oct.) 1938. Long, Bliss and Feinstone.[15]

35. Finland, Maxwell; Brown, J. W., and Rauh, A. E.: Treatment of Pneumococcic Meningitis, New England J. Med. **218:** 1033 (June 23) 1938.

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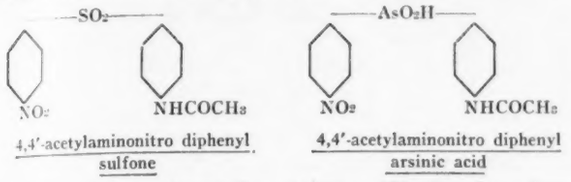
38. Fourneau, E.; Trefouel, J.; Nitti, F., and Bovet, D.: Action antistreptococcique des *p*-aminophenyl-alcoylsulfones et quelques dérivés voisins, Compt. rend. Soc. de biol. **127:** 393, 1938; Bull. Acad. de Med. **118:** 210 (Oct. 5) 1937.

39. Levaditi, Constantin; Girard, André, and Vaisman, Aaron: Chimiothérapie des infections expérimentales par la diacetyldioxydiphenylsulfone, Compt. rend. Soc. de biol. **127:** 19, 1938.

That sulfur is not essential for activity has been shown by Rosenthal and Bauer [40] in that asymmetrical arsenic derivatives analogous to the sulfones



possess antistreptococcic action. We [40] also found simultaneously with Mayer and Oechslin [41] that *p*-nitrobenzoic acid

has a slight action against pneumococcic and streptococcic infections in mice. These brief examples serve to illustrate the wide chemical front along which the conquest of bacterial infections may be approached.

A survey of the numerous derivatives brings out the importance of an amino or nitro group in the para position in the benzene ring. Substitutions in the amino group of sulfanilamide are much more prone to diminish antibacterial activity than substitution in the sulfonamide group. Mayer [42] has found that an intermediate oxidation product of the amino group, the hydroxylamine (NHOH) derivative of sulfanilamide, is highly active in the test tube against streptococci. Mayer has postulated the slow formation in the body of this derivative as the basis for activity of sulfanilamide. The hydroxylamine derivative as such (*p*-hydroxylamino-benzene sulfonamide) is unstable when injected into the body; the feeble therapeutic activity shown when this compound itself is employed is believed by Mayer to be due to its rapid breakdown. Mellon and

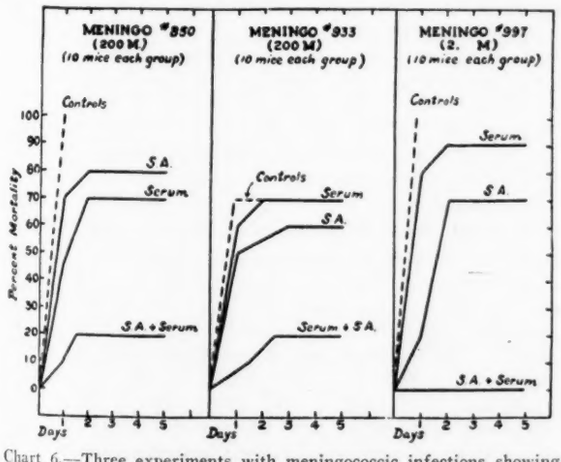


Chart 6.—Three experiments with meningococcic infections showing the marked curative effects of combined drug and serum therapy when each alone yielded poor results; treatment subcutaneously two hours after infection with 0.8 Gm. per kilogram of sulfanilamide and 0.5 cc. of 1:5 dilution of meningococcic serum.

his co-workers [43] have also suggested that the hydroxylamine derivative may be the active agent by virtue of its anticatalase activity.

Following the administration of sulfanilamide, not all of the compound can be recovered as the free or acetylated derivative.[1] It is thus of importance to know more of the fate of that portion of the drug which is unaccounted for.

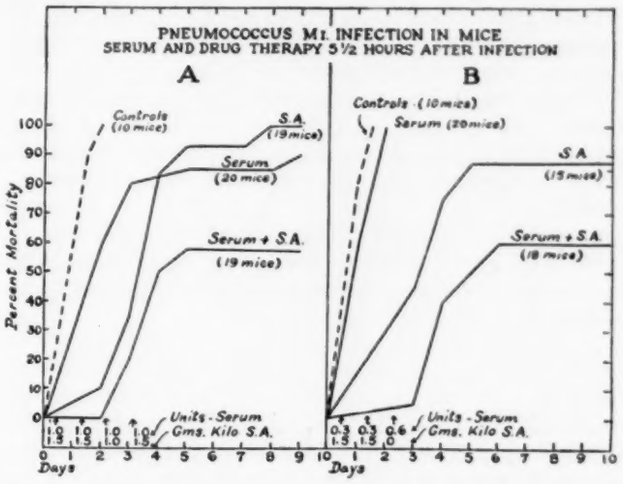


Chart 7.—The increased effectiveness of combined drug and serum therapy in type I pneumococcic infection in mice. Treatment subcutaneously begun five and one half hours after inoculation. Units of serum (Felton) and dosage of sulfanilamide are indicated by arrows on the chart.

We [44] have recently devised tests for the estimation of aromatic hydroxylamines and for further oxidation products of aromatic amino groups, that can be carried

Presence in Urine of an Hydroxylamine Derivative of Sulfanilamide Following Oral Administration of 1.5 Gm. of Sulfanilamide in 100 Cc. of Water to Two Rabbits of 2.8 and 2.65 Kg. Weight

	Urine Volume	Free Sulfanilamide	Total Sulfanilamide	Hydroxylamine Sulfanilamide
2 hrs.	30 cc.	30 mg.	60 mg.	0.45 mg.
4 hrs.	93 cc.	93 mg.	177 mg.	2.14 mg.
6 hrs.	25 cc.	87 mg.	188 mg.	2.4 mg.
2 hrs.	52 cc.	52 mg.	78 mg.	1.0 mg.
4 hrs.	45 cc.	45 mg.	95 mg.	2.1 mg.
6 hrs.	28 cc.	56 mg.	126 mg.	2.8 mg.

out in the presence of sulfanilamide or other aromatic amino compounds. Following the administration of sulfanilamide to rabbits, it has been possible to demonstrate from 1.5 to 5 per cent of the free sulfanilamide in the urine present as a compound giving the reactions characteristic of the hydroxylamine derivative (shown in the accompanying table).[45] This of course does not finally prove that the hydroxylamine derivative is the active agent, but it should now be possible to correlate the presence of this compound with bacteriostatic effects and to investigate further the relation of hydroxylamine derivatives and of further oxidation products of the amino group to toxicity and to therapeutic activity.

SUMMARY

The acute toxicity of sulfanilamide and related compounds is no reliable index of the toxicity to be encountered on continued administration, particularly under adverse conditions of infection or dietary restriction. Variations in the toxic manifestations of sulf-

40. Rosenthal, S. M., and Bauer, Hugo: Studies in Chemotherapy: IX. Antibacterial Action of Some Aromatic Arsenic, Sulfur and Nitro Compounds, Pub. Health Rep. **54:** 1317 (July 21) 1939.

41. Mayer, R. L., and Oechslin, C.: Sur une nouvelle classe de corps antibacteriennes: l'acid p-nitrobenzoique et ses esters, Compt. rend. Soc. de Biol. **130:** 211, 1939.

42. Mayer, R. L.: Recherches sur le mécanisme de l'action antistreptococcique de l'aminobènzenesulfamide et ses dérivés, Bull. Acad. de méd. **117:** 727 (June 22) 1937.

43. Shinn, L. E.; Main, E. R., and Mellon, R. R.: Anticatylase Activity of Sulfanilamide and Related Compounds: II. Relation to Growth Inhibition in Pneumococcus, Proc. Soc. Exper. Biol. & Med. **39:** 591 (Dec.) 1938.

44. Rosenthal, S. M., and Bauer, Hugo: Studies in Chemotherapy: X. Colorimetric Tests for Aromatic Hydroxylamines and for Further Oxidation Products of Aromatic Amines, Pub. Health Rep. **54:** 1880 (Oct. 20) 1939.

45. Similar reactions have also been obtained in the urine of dogs, of rats and of man following sulfanilamide administration.

anilamide occur in different species of animals. There is inadequate knowledge of the chronic toxic effects on laboratory animals.

Relatively large doses of sulfanilamide and repeated therapy are required to bring about a high percentage of cures in streptococcic infections in mice.

With pneumococcic infections, marked variation in response to therapy occurs with different species of animals.

Combination of sulfanilamide therapy with specific antiserum in pneumococcic, meningococcic and streptococcic infections in mice brings about more favorable results than those obtained with either type of therapy used alone.

It has been shown that sulfur is not essential to therapeutic activity. Antibacterial properties have been demonstrated for some aromatic arsenic compounds, as well as for *p*-nitro benzoic acid.

Following the oral administration of sulfanilamide to rabbits, a small percentage of an oxidation product of the amino group (hydroxylamine) has been detected in the urine. Other investigations have suggested the possible significance of this derivative in the mechanism of action of sulfanilamide.

ABSTRACT OF DISCUSSION

ON PAPERS OF DR. KING ET AL. AND DR. ROSENTHAL

DR. CHARLES L. FOX JR., Boston: The paper of Dr. King and his co-workers is interesting but I would make one observation to be considered in evaluating some of his facts. Hourly bacterial counts of cultures with sulfanilamide (10 mg. per hundred cubic centimeters) and controls without sulfanilamide show these three features: For the first three hours growth is equal in the two. Then the control proceeds along the logarithmic phase of growth whereas the sulfanilamide culture grows but slightly until the eighth or ninth hour. Then this period of bacteriostasis (from the third to the ninth hour) ends and the sulfanilamide culture grows out equaling the control. If, therefore, one has not observed the culture between about three hours and about eight hours, one is likely not to see any bacteriostatic effect whatever. In table 5 which Dr. King showed, and in all his observations, I believe the first observation of the colony was at nine hours. His other observations were at about twelve hours. If one considers this fact, one will recognize that the major effect of the drug occurs between about the third and the ninth hour, but after nine hours one is not going to see so much effect. It may be possible to recognize that a culture the growth of which has been held up for three or four hours here at this time, at about seven or eight hours, is a younger and possibly a more actively growing culture than the control which has been growing vigorously during that period. There may be a possibility that this increased hemolytic effect of the organism grown in sulfanilamide is due to the fact that his observations, beginning at about nine hours, are on cultures with controls which are not growing as actively at this stage as the sulfanilamide cultures. In evaluating all sulfanilamide studies, I think it must be realized that the major effect of the drug occurs between about the third and the ninth hour.

DR. SANFORD M. ROSENTHAL, Washington, D. C.: I think we are all on the right track in mechanism, but I just want to add that most of our work has been in the test tube and that all mechanisms of action based on in vitro experiments remain theories until they are demonstrable in the living organism. I feel that we now have to take our test tube work over into the animals to see whether the same thing applies. I should like to ask Dr. Shinn whether he has studied the blood of animals or human beings under sulfanilamide for the catalase activity or for peroxide content.

DR. JOSEPH T. KING, Minneapolis: The question was raised by Dr. Fox whether with this method one might overlook an important phase of the bacteriostatic action of sulfanilamide during the early part of the incubation period. Since the diameter of the colony is used as the index of growth rate in this medium, no information exists concerning growth until the colonies can be measured microscopically. In the medium without erythrocytes the colonies usually appear between the fourth and the sixth hour of incubation. On the basis of colony diameter the maximal bacteriostatic effect of the drug occurs at a point in time later than that at which colonies become measurable in both experimental and control cultures. Dr. Fox also pointed out that, although the growth curve of cultures containing sulfanilamide is usually greatly retarded in the early part of the incubation period, it may eventually rise above the control and he raised the question whether this might account for the higher hemolytic index observed in our cultures. With my technic I usually observe a decrease in the bacteriostatic action of the drug following the maximum, which usually occurs somewhere near the twenty-four hour period. This tendency is probably more pronounced when the cultures contain erythrocytes. I have never observed the bacteriostatic action to fail completely—the experimental colonies never become larger than the controls in this medium. This fundamental difference between fluid mediums and tissue culture clots where the organisms grow as colonies must be kept in mind when interpreting results. In any event this suggestion could hardly account for the fact that a higher hemolytic index is found in cultures containing sulfanilamide, since this term expresses the hemolyzing power of a colony in relation to its size, i. e. the diameter of the hemolytic zone divided by the diameter of the colony. The absolute amount of hemolysis is less in experimental cultures than in controls. The experimental colonies produce wide zones of hemolysis in relation to their size.

L. E. SHINN, PH.D., Pittsburgh: With regard to the paper of Dr. Rosenthal, I am glad to see some one embark on a study of compounds other than the interminable ringing of changes on the amino attached to the sulfur. So far as I know, no one has made any systematic efforts to get at the real fundamentals of the structure, replacing the sulfur with other substances and making the changes in the heart of the molecule, so to speak. We have begun work similar to that which he has discussed with regard to the benzoic acid. I am preparing to do some work on arsenicals in the belief that that group, the group which is now the sulfonamide group, is not in itself particularly important or critical. From my point of view, the action of that group probably lies in its influence on the amino group. Its effect is indirect, unstabilizing the amino group to just the right degree. Dr. Rosenthal asked whether I had examined the tissue fluids of animals or human beings with regard to the anticatalase mechanism, production of hydroxylamine, and so on. I must say that I have not. I had considered it hopeless to hunt for the hydroxylamine derivative in vivo. The question was raised as to what is going to be done with some other organisms—the staphylococcus, the diphtheria bacillus, B. coli and the gonococcus. On that question I cannot say very much. I feel that we are going to find in those organisms factors which will allow the application of this or a very similar theory in explanation of mechanism. For example, the gonococcus is presumed to be a producer of an appreciable amount of catalase and, since it is a producer of catalase, one must presume that that catalase serves some purpose. The indication would be that the organism is extremely susceptible to hydrogen peroxide and therefore that interference with catalase may be even more effective.

DR. I. S. RAVDIN, Philadelphia: The workers who believe that anticatalase activity is responsible for the mode of action of sulfanilamide must explain why this drug is effective against the colon bacillus, which grows well in the presence of hydrogen peroxide. The explanations advanced this morning must not be accepted as proofs of the mode of action of these very interesting and useful substances but further work must be awaited.

DR. FOX: Dr. Rosenthal said he would like further evidence as to the presence in the blood of patients or animals of some of these compounds which assumedly are formed from sulfanilamide in vivo. That evidence has been difficult to get.

We have taken specimens of blood of sulfanilamide treated patients and, by using the recording spectrophotometer at the Massachusetts Institute of Technology, have been able to get a smooth line curve of the transmission spectrum of the blood of these patients. Such blood almost always contains methemoglobin, as many others have shown, and sometimes sulfhemoglobin, but, in addition, in the red end of the spectrum, where hemoglobin absorbs but slightly, there is a residual absorption. The human eye is but slightly sensitive, and the ordinary spectrophotometer is less accurate in the region above 650 millimicrons. With the recording spectrophotometer we have gone from 400 to 700 millimicrons. From about 650 to 700 millimicrons there is definite absorption strikingly similar to the absorption by the products of the ultraviolet irradiation of sulfanilamide. Important additional evidence for the presence of these oxidation products in patients' blood is that, added in vitro, these products convert hemoglobin to methemoglobin. Sulfanilamide itself has absolutely no such effect. Dr. Rosenthal said that the compound nitrosobenzene, the oxidized form, is bacteriostatic. I have found that addition of a paradimethylamine group produced a compound 100 times more bacteriostatic than nitrosobenzene. These substances are reversible oxidizing systems and in vitro, in mice, produce fatal methemoglobinemia so that therapeutic tests were unsuccessful.

SEROLOGIC DISCREPANCIES IN SYPHILIS

THE POSITIVE HINTON-NEGATIVE WASSERMANN PROBLEM

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AND
LEON F. RAY, M.D.
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The occurrence of a positive Hinton with a negative Wassermann reaction in patients with late syphilis gives rise to delicate problems of diagnosis as well as to the question of activity in old cases and the advisability of further treatment. The first technic of the Hinton test [1] was adopted for routine use at the Massachusetts General Hospital in 1929. The present method,[2] which is comparable to the Eagle, Kahn, Kline and Kolmer tests as to specificity and surpasses them in sensitivity,[3] is similar in principle to the Eagle, Kahn and Kline tests. When the Hinton test was first used at the Massachusetts General Hospital it was applied to all bloods in conjunction with the Wassermann test. The technic of the latter test is a modification of the standard Wassermann test.[4] A general agreement between the two tests led to the practice of omitting the Wassermann test unless the Hinton test was positive. When an additional check was desired, a portion of the specimen was sent to the Massachusetts State Board of Health Laboratory, where the Hinton technic is under the supervision of its originator. With the passage of time, however, cases exhibiting a disagreement between the two tests gradually accumulated.

In new infections, the development of increased sensitivity in tests for syphilis facilitated diagnosis. In late syphilis, however, more delicate tests increased the importance of demonstrating clinical evidence of the disease. The specificity of blood serologic reports might otherwise be open to question. The results of nationwide serologic conferences for evaluation by the United States Public Health Service indicate that these highly sensitive technics are accurate. The extensive application of such methods of blood examination has given rise to many intricate and perplexing problems. Some doubts arose when new technics produced a positive reaction accompanied by a simultaneous negative report with an older standard test. In early syphilis "serologic cures" were delayed, with a corresponding increase in serofast cases. In late syphilis, especially the asymptomatic group, still more difficulties appeared. It was questioned whether persistently positive serologic examinations by such delicate technics meant continued activity of the disease. Criteria of adequate therapy were consequently open to further consideration. Many old Wassermann-negative cases exhibited positive reactions to the new tests. Likewise, numerous unsuspected cases appeared which were negative by older methods. Some clinicians doubted that a positive report by such sensitive procedures meant syphilis in the face of a negative Wassermann reaction unless other evidence was provided. Cannon [5] stated that a properly controlled "4 plus" Wassermann reaction meant active syphilis in need of treatment, with certain exceptions including yaws and leprosy. Can his statement be applied as well to the more sensitive tests? Kolmer [6] expressed the opinion that serologic positivity in an apparently healthy person, even with previous adequate therapy, indicated the persistence of syphilitic infection. He further stated that serologic relapse meant renewed activity of foci of the disease. Kolmer also indicated that therapy was needed to aid immunity and prevent progression of the disease. Can such beliefs be applied to cases exhibiting a positive serologic reaction by sensitive methods when the Wassermann reaction is negative? The questions are partially answered by the ratings of accuracy attained by many of the sensitive tests in the reports of serologic congresses. We have attempted to clarify some of these problems from the clinical aspect by the following work.

DATA

In the period from July 1936 to July 1938 there were 2,862 new admissions to the syphilis clinic at the Massachusetts General Hospital. Excluding early syphilis, there were 335 cases (11.7 per cent of the total) which were found to have a positive Hinton and a negative Wassermann reaction on the first blood serologic examination. During the same period 1,078 cases of syphilis were diagnosed, so that these 335 patients comprised 31 per cent of the actual cases of syphilis admitted. This group was chosen for the present study without further criteria of selection. Early syphilis of less than two years' duration was excluded because such cases would present more of a question of adequacy of therapy than a serologic problem. During the same period of time approximately 40,000 specimens of blood

From the Massachusetts General Hospital, Department of Dermatology and Syphilology, Dr. C. Guy Lane, chief.
Read before the Section on Dermatology and Syphilology at the Ninetieth Annual Session of the American Medical Association, St. Louis, May 18, 1939.

1. Hinton, W. A.: A Glycerol-Cholesterol Precipitation Reaction in Syphilis, Boston M. & S. J. **196**: 993 (June 16) 1926.
2. Hinton, W. A.: Syphilis and Its Treatment, New York, Macmillan Company, 1936, p. 293.
3. Cummings, H. S.; Hazen, H. H., and others: The Evaluation of Serodiagnostic Tests for Syphilis in the United States, Report of Results, Ven. Dis. Inform. **16**: 189 (June) 1935 (first evaluation). Parran, Thomas; Hazen, H. H., and others: The Efficiency of State and Local Laboratories in the Performance of Serodiagnostic Tests for Syphilis, ibid. **18**: 4 (Jan.) 1937 (second evaluation). Parran, Thomas; Hazen, H. H., and others: A Comparative Study of Serodiagnostic Tests for Syphilis, ibid. **18**: 273 (Aug.) 1937 (third evaluation).
4. Mallory, F. B., and Wright, J. H.: Pathological Technique, Philadelphia, W. B. Saunders Company, 1924, p. 533.
5. Cannon, A. B.: The Tracing of Syphilis Through Common Ailments, J. A. M. A. **109**: 348 (July 31) 1937.
6. Kolmer, J. A.: Serologic Reactions and Immunity in Relation to Infection and Treatment of Syphilis, Am. J. Syph., Gonor. & Ven. Dis. **22**: 426 (July) 1938.

were tested in the hospital laboratory; 21,073 of these were on new cases admitted to various departments. By a thorough investigation of the 335 patients with late syphilis exhibiting a positive Hinton and a negative Wassermann reaction, it was hoped that a base line could be established as to the meaning of such a serologic status. They were considered especially in the light of diagnosis, activity of syphilis and need of further treatment. At the outset relatively few cases presented distinct evidence of syphilis; the positive Hinton reaction was the only reason for observation of the remainder. In many instances the actual presence of the disease was seriously doubted. After more careful history taking, physical examinations, repeated serologic checks and other diagnostic measures, definite additional proof of syphilis appeared in nearly half of the cases. The final grouping of the series appears in table 1. The diagnosis of syphilis was made in groups A, B and C, in which each patient had three or more positive Hinton reactions. In groups D and E there was disagreement in blood reports. Each group will be considered separately.

TABLE 1.—*A Study of the Positive Hinton-Negative Wassermann Problem*

	Number of Cases	Per Cent
A. Positive Hintons plus positive evidence of syphilis	155	46.3
B. Positive Hintons plus suspicious evidence of syphilis	36	10.7
C. Positive Hintons plus no evidence of syphilis	54	16.2
D. Doubtful or undecided cases	42	12.5
E. Not syphilis	48	14.3
Totals	335	100.0

TABLE 2.—*Bases of Diagnoses in Group A*

Three or more positive Hinton reactions plus:	No. of Cases
1. History of syphilis	63
2. Physical evidence	8
3. Positive Wassermann	11
4. History and physical evidence	32
5. History and positive Wassermann	18
6. Physical and positive Wassermann	5
7. Physical and positive spinal fluid	8
8. History, physical evidence and positive Wassermann	6
9. History, physical evidence and positive spinal fluid	4
Total	155

GROUP A.—In this group of 155 patients positive evidence of syphilis was found, each case averaging 2.4 indications of the disease in addition to the positive Hinton reaction. In the history the additional evidence consisted of a story of a primary sore, secondary manifestations, tertiary lesions, disturbances of the central nervous system, miscarriages, stillbirths, interstitial keratitis or previous therapy. The family history included known syphilis in the husband or wife, child, sibling or parent. On physical examination the additional signs consisted of mucocutaneous scars, osseous lesions (septal perforations, saddle nose, dental changes and Charcot's joints), ocular lesions (pupillary changes, interstitial keratitis, optic atrophy, choroiditis), neurologic lesions (other than ocular) and cardiovascular syphilis. Laboratory evidence of syphilis other than the positive Hinton reaction included subsequent positive Wassermann reports, positive changes in the cerebrospinal fluid, x-ray evidence of syphilitic cardiovascular lesions and one autopsy showing syphilis. When all the evidence was gathered, analysis revealed that the diagnoses were made as indicated in table 2.

The average age of these 155 patients was 43.7 years. In ninety-six cases in which the duration was known the disease had been present for an average of 23.7 years. There were twenty-five patients with congenital syphilis whose average age was 24.7 years. Among the 130 patients with acquired syphilis were seventy-nine males with an average age of 50.4 years; the ages of fifty-one females averaged 42.3 years. Further study of the latent, active and congenital subdivisions revealed some pertinent information: It was of interest to note that of thirty-nine patients with evidence of activity of the disease the average duration in eighteen known instances was 21.5 years. Among ninety-one inactive cases, the average duration in fifty-three in which onset was known was 25.3 years. These figures support those observers who feel that syphilis does not actually become "latent" and that some therapy, if tolerated, should be continued as long as there is detectable reagin in the blood. Also it was found that the thirteen patients with active congenital syphilis averaged 25.3 years of age. This is indicative of the necessity of lengthening the time wherein many observers feel that active syphilis exists. We are inclined to agree with those who believe that there is no time, regardless of the duration of the infection, at which syphilis may be trusted to remain inactive. This may apply to congenital as well as to acquired cases. The older group of patients with congenital syphilis should not be therapeutically neglected merely because they have grown to maturity without disabling lesions.

The effect of previous treatment is illustrated in table 3. These calculations bear out the already proved fact that any treatment is better than none. Among the untreated cases 33 per cent were active, whereas of those with even less than twenty-five injections less than 15 per cent showed active syphilis. This group of cases, wherein much confirmatory evidence was found, illustrated not only the value of routine serologic tests of the blood but also the importance of a good follow-up in establishing a diagnosis of syphilis.

TABLE 3.—*Results of Previous Treatment*

Amount of Treatment	Active Cases	Inactive Cases	Total Cases
Twenty-five or more injections	7	38	45
Less than 25 injections	5	29	34
None	25	51	76

TABLE 4.—*Group B: Bases of Diagnoses*

Four or more positive Hinton reactions plus:	Cases
1. History suggesting syphilis	15
2. Physical conditions suggesting syphilis*	9
3. Suspicious history and physical evidence	12
Total	36

* Two cases also showed roentgenologic evidence suggesting cardiovascular syphilis.

GROUP B.—The thirty-six patients in this group all had four or more positive Hinton reactions and presented in addition some suggestive evidence of syphilis. The blood Wassermann reaction remained negative in all cases. A summary of this group is presented in table 4.

The average age of group B patients was 47.1 years. Since the history and physical evidence were not conclusive, cases of congenital syphilis could not be definitely segregated. A suggestive history consisted of dubious genital lesions, indistinct eruptions, possible iritis, and miscarriages or stillbirths of doubtful significance. There was a suspicion of syphilis in some member of the family in one fifth of these cases.

TABLE 5.—*Group B: Additional Studies*

	Cases
1. Corroboration of positive Hinton by other laboratories	25
2. Spinal fluid examinations (all negative)	19
3. Cardiovascular x-ray studies (2 suspicious and 8 negative)	10

TABLE 6.—*Group C: Additional Studies*

	Cases
1. Corroboration of positive Hinton reaction by state laboratory	35
2. Spinal fluid examinations (all negative)	28
3. Cardiovascular x-ray studies (all negative)	12

Indecisive physical lesions were inconclusive scars, osseous changes, dental changes, facies, pupillary aberrations, dubious old choroiditis or optic atrophy, other suspicious neurologic lesions, questionable cardiovascular damage and gastritis. Additional investigations are given in table 5.

GROUP C.—The fifty-four cases included here were diagnosed as syphilis on the basis of persistently positive Hinton reactions alone. This seemed justified in the light of such observers as Moore,[7] who stated that, if a precipitation test is reliable, a series of positive reactions must be considered of the same significance as a series of positive Wassermann reactions. The Hinton test appeared to fulfil this criterion and should mean syphilis when persistently positive, regardless of negative Wassermann reactions. Five or more positive reactions were obtained here in each case; no evidence other than this was afforded. The average age in this group was 46.3 years. Additional investigations are given in table 6.

After having studied and tabulated the first two groups of cases (A and B) there was no hesitancy in our minds about making a diagnosis of syphilis in group C. Yaws and leprosy could be eliminated without difficulty; malaria was ruled out as far as possible by the anamnesis. The five blood examinations which gave consistently positive results were done over an average period of 9.8 months in all cases. This time factor should rule out the few diseases which are thought to cause a temporary positive reaction. The cases in this group comply with the criteria generally used to denote true latent syphilis.

GROUP D.—In this group there were forty-two cases that have not been classified. It was impossible to decide whether these patients had syphilis or were free of the disease. After the initial positive Hinton reaction the reports vacillated repeatedly. There was nothing in the personal or family history to suggest syphilis, nor was there a story of any disease which might have given rise to a "false positive" report. No physical evidence was found to suggest syphilitic damage. The average age was 40.2 years. These patients have been followed for an average period of 10.2 months each. A summary of the data in this group appears in table 7.

Disagreements in the blood serologic reports were pronounced in this group. Additional checking by sending split samples simultaneously to two laboratories did not settle the question in these cases because of the failure of the results to coincide. This fact is demonstrated in table 8.

An example of the type of case encountered in this group is given in table 9.

It is possible that many of these patients had syphilis and perhaps some did not. From the clinical standpoint there was no way to decide. From a purely serologic aspect the discrepancies in reports precluded an accurate decision. It seemed that ten months should be long enough in which to decide whether most patients had syphilis, but when the data given were considered from the practical point of view the problem was not always clear.

GROUP E.—It was felt that in all probability the forty-eight patients in this group did not have syphilis. In each case there was a single positive Hinton reaction followed by several negative reactions. The initial positive reaction was followed by three or four negative reactions over a period of 10.5 months average time. Here again there was no history or physical evidence of syphilis in any case. The average age was 38.4 years. Every attempt was made to rule out any condition which might possibly have given rise to a temporary false report, since haptens or "partial antigens" are thought to cause such reactions in some diseases. Table 10 presents the data on these patients. Serologic discrepancies were less pronounced in this group, as is reflected in table 11.

The question of "false positive" reactions arose in this group, and the series of subsequent negative tests in these cases indicated such a situation. These forty-eight patients comprised 13.7 per cent of the 335 cases

TABLE 7.—*Group D: Forty-Two Undecided Cases with Serologic Discrepancies*

Blood Serologic Data	Average No. per Case
1. Positive Hinton reactions	2.1
2. Doubtful Hinton reactions	0.6
3. Negative Hinton reactions	3.1
Total average number of tests	5.8

Additional Studies	Cases
1. Hinton test done by state laboratory	31
2. Spinal fluid examinations (all negative)	16
3. Cardiovascular x-ray studies (all negative)	4

TABLE 8.—*Comparison of Discrepancies in Two Laboratories in Group D**

	Cases
State laboratory (31 cases)	
1. Hinton positive	7
2. Hinton negative	24
3. Subsequent disagreement in the same laboratory	5
Massachusetts General Hospital laboratory (42 cases)	
1. Hinton positive	40
2. Hinton negative	2
3. Subsequent disagreement in the same laboratory	36

* Discrepancies between reports from the two laboratories occurred in twenty-four cases.

7. Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., Charles C. Thomas, 1933, p. 465.

studied, which was an undue number of false positive reactions for a test which has stood high in the conferences on serologic tests recently held. When computed on the basis of the state laboratory reports alone, in which only three positive reactions were obtained, less than 1 per cent of false positive reactions would exist. This was in agreement with the accepted status of the Hinton test. Some degree of error exists, however, in that not all cases were checked by the state laboratory. This situation implies that the Hinton test

TABLE 9.—*Example of Case in Group D*

History: L. A., a man aged 42, in February 1938 complained of discomfort in the lower part of the abdomen of 4 years' duration; the past, family and marital histories were entirely negative for syphilis	Date	Serologic Tests: Hinton	Serologic Tests: Wassermann
Physical examination: Three complete physical examinations by three different physicians over a period of 10 months were entirely negative for clinical evidences of syphilis	2/ 8/38	Pos.	Neg.
	2/11/38	Pos.	Neg.
	3/ 5/38	Pos.	Neg.
Laboratory studies:		(State)	
Spinal fluid:	3/ 5/38	Neg.	
Cells 0			
Total protein 21			
Wassermann reaction negative	3/10/38	Pos.	Neg.
Colloidal gold curve 0000000000			
Blood counts, urine and stool were normal	5/31/38	Neg.	Neg.
Gastrointestinal and cardiovascular x-ray studies were negative			
Gastroscopic examination showed superficial and hypertrophic gastritis	7/ 7/38	Pos.	Neg.
Serologic examination on wife negative	12/10/38	Neg.	Neg.

as done in the laboratory at the Massachusetts General Hospital was lacking in specificity. A tabulation of the chronologic occurrence of these false positive reactions, compared with the number of reports received per month, showed a direct ratio of incidence. That is, more were found in those months during which most of the cases were picked up.

This group showed the value of comparative serologic data between laboratories, even for the better hospitals. It also emphasized the absolute necessity of checking and rechecking a positive serologic reaction of the blood when other evidence is lacking.

"FALSE POSITIVES"

In order to compute the true percentage of false positive reports it was necessary to use the total number of new bloods tested in the laboratory during the

TABLE 10.—*Group E: Forty-Eight Patients Not Having Syphilis*

Blood Serologic Data	Average No. per Patient
1. Positive Hinton tests	1.0
2. Doubtful Hinton tests	0.2
3. Negative Hinton tests	4.0
Total average number of tests	5.2
Additional Studies	**Cases**
1. Hinton test done by state laboratory	34
2. Spinal fluid examinations (all negative)	4
3. Cardiovascular x-ray studies (all negative)	9

twenty-four months which this study included. There were 21,073 new patients who had serologic examinations of the blood during this time. To allow for the widest possible margin of error, all of both groups D and E were included, which made a total of ninety possible cases, which would be 0.42 per cent of false positives. The total number of positive and doubtful reports on these ninety patients was 171. If computed on the basis of this number of tests against the total number of blood specimens examined by the laboratory during this period, approximately the same percentage of false positives is calculated.

The occurrence of false positive reactions can be attributed with certainty to such oriental diseases as yaws, relapsing fever and trypanosomiasis. Leprosy and malaria show false positive reactions less often. Hyperpyrexia, hemorrhagic diseases and jaundice are highly controversial. All these conditions were ruled out as far as possible in the present study. When a case showed occasional positive results interspersed among several negative ones, it may have been due to a fluctuating and very low reagin titer. Some good authorities construe such cases as being definitely syphilitic. Other observers feel that these serums contain some unknown substance which may be detected by a given test and that in the absence of clinical corroboration there is no syphilis present. There were nineteen cases in group D which exhibited this vacillating type of serologic status. Perhaps these were the only truly false positive cases. The rest of group D showed two

TABLE 11.—*Comparison of Hinton Reports from Two Laboratories*

	Cases
State laboratory (34 cases)	
1. Hinton positive	3
2. Hinton negative	31
3. Subsequent disagreement in the same laboratory (Two positives later negative, one not repeated at state laboratory)	2
Massachusetts General Hospital laboratory (48 cases)	
1. Hinton positive	46
2. Hinton negative	2
3. Subsequent disagreement in the same laboratory (All positives later repeatedly negative)	46
Discrepancies between the two laboratories	34
No case positive in both laboratories	
Only 2 cases positive at state laboratory and negative at Massachusetts General Hospital laboratory	

or more positive or doubtful reactions followed by several negative reactions. It is possible that such patients showed a fading reagin titer just at the time at which it passed below a detectable level. A mistaken report or technical error occurring twice per case seemed most unlikely in so many instances.

The cases in group E, however, were in all probability merely falsely positive in the sense of "technical errors." A single positive reaction was followed by repeated negative reactions in each instance. Possible disease causes of a temporary false positive reaction were ruled out. Technical errors in such cases may be due to improper technic in the performance of the test, the skill of the individual technician, human fallibility in reading the tests, errors in labeling the tubes and mistakes in reporting the results. The occurrence of only forty-two such cases among 21,073 new serologic examinations provided the extremely low figure of 0.2 per cent in the two year period. Other situations that give rise to false positive or anticomplementary reactions in the complement fixation tests do not need to be considered here. These include bacterial or chemical contamination, the presence of a high concentration of a drug in the serum and an excess of native amboceptor. Many such factors which may inhibit complement fixation have no effect on the flocculation phenomenon and hence may be disregarded.

SUMMARY

Of 2,862 new patients admitted to the syphilis clinic at the Massachusetts General Hospital in a two year period, 335 late cases showed a positive Hinton and a negative Wassermann reaction. This group was studied exhaustively for additional evidence of syphilis. Nearly 50 per cent of these patients were found to exhibit a history or physical or laboratory evidence of the disease along with a repeatedly positive Hinton reaction. Another 25 per cent of these patients were diagnosed as syphilitic on the basis of a persistently positive Hinton reaction alone. In 12.5 per cent of the 335 cases a vacillating serologic reaction and lack of other evidence created indecision as to the presence or absence of syphilis. In the remaining 14.3 per cent of these cases the one initial positive reaction followed by repeated negative reactions was held to be a technical error.

The average age of the entire group was 42.8 years. The known average duration of syphilis in the clinically active group was 21.5 years in acquired cases. The average age of congenital syphilitic patients with active disease was 25.3 years, the eldest of whom was 30.

False positive reports were computed to allow for the widest possible margin of error. All undecided cases and all technical errors were included. Comparing this number to all new specimens examined by the laboratory during the time of the study, a figure of 0.42 per cent of false positives was obtained. This corroborated clinically the high degree of specificity attained by the Hinton test in congresses on serologic tests.

ABSTRACT OF DISCUSSION

DR. C. GUY LANE, Boston: The paper of Dr. Crawford and Dr. Ray adds to the evidence, if any is necessary, of the value of serologic tests in the detection of syphilis. Secondly, this work indicates the frequency with which confirmatory evidence can be found on careful study. We are impressed with the development of other manifestations of syphilis when patients with positive serologic reaction are examined carefully, and the authors have given us additional evidence of the possibility of the detection of such manifestations. In this particular series, some 50 per cent of the cases in which a positive serum reaction of the blood is present in the beginning can be taken out of the group of latent cases and diagnosed as symptomatic tertiary cases by the finding of other evidence. These figures also emphasize the importance of the latent group of syphilis today. While there are only some 14 per cent of true latent cases in this series, a review of the records in our clinic at the Massachusetts General Hospital over a five year period in which some 2,800 cases have been diagnosed as syphilis discloses that about 1,600, or 60 per cent, are diagnosed as latent syphilis. This study also shows again the unreliability of a single serologic examination. This fact must be reiterated to general practitioners, to other physicians and to the public as well. A press release of the Public Health Service the other day depicted premarital and antepartum serologic examination or blood test without reference to other examination or the need for checking up on those particular tests. The same flaw appears in the premarital and antepartum laws in the various states. There should be equal emphasis at least on further examination and further check-up of cases in which a single serologic positive is found. Finally this paper emphasizes the desirability of more than one type of test in our judgment of cases. For example, take the figures of our own clinic, with about 1,000 cases a year admitted for examination with reference to syphilis. Here are about 350 cases of serologic discrepancy in a two year period, a rather large percentage of cases in which a discrepancy has arisen. Therefore a test by a second method is of value in that it may in the first place aid the diagnosis by agreement; secondly, the second test may point to the diagnosis by the development of other evidence perhaps because of the mere positivity of the second test and a negativity of the first test; and thirdly, the mere fact of the disagreement between the two tests may lead to a further detailed examination which may be entirely negative, and therefore the patient can be discharged because of the lack of evidence.

DR. G. V. KULCHAR, San Francisco: Drs. Crawford and Ray have well emphasized the necessity for repeated serologic examinations for the diagnosis of syphilis in the absence of clinical evidence. That is a fact that needs reemphasis. One would expect every case that gives a positive Hinton reaction to give a positive Wassermann reaction. This is not true, and it is explainable on the fact that the Hinton test as shown by the serologic ratings is much more sensitive than some of the older Wassermann tests. Does a positive Hinton reaction always mean syphilis? I have shown that there is a reagin-like substance in the serum of normal persons. Accepting that, it seems conceivable, though the data are not convincing as yet, that some intercurrent condition such as diabetes, menstruation or infectious mononucleosis fever may cause an increase in this reagin substance such as occurs following the injection of neoarsphenamine in nonsyphilitic persons to bring it up well within the range of positivity to the ordinary serologic test. I think this may explain the positive, transitory positive Wassermann reactions that are observed during febrile states, in tuberculosis, and particularly in diabetes, in infectious mononucleosis. There is another angle. The frequent positive Wassermann reaction noted in malaria in the absence of syphilis is thought to be due to a reversal of the normal serum albumin-globulin ratio. A reversal of this serum albumin-globulin ratio, of course, takes place in other diseases. Changes in the serum albumin-globulin ratio occur in lymphopathia venereum. Lymphopathia venereum is one of the diseases reputed to have given a false positive Wassermann reaction. So we must look on the Wassermann test not as a specific but as a nonspecific test, which, like all nonspecific tests, is subject to error. Does a positive Hinton reaction necessarily mean active syphilis in a syphilitic patient? Now the studies of the Cooperative Clinical Group I think have indicated pretty definitely the benignity of late latent syphilis. Taking this along with the studies of Bruusgaard, there seems no great need of treating patients in late latency. In a person who is first seen twenty years or more after his infection, in whom the cerebrospinal fluid is negative, who is long past his period of infectivity and who through fluoroscopy and as far as one can go through physical examination presents no evidence of cardiovascular syphilis, we know his chances of developing a serious lesion from syphilis are relatively slight. So it does seem rather unnecessary to subject these patients to the hazards of treatment. Their possibilities of going through life without any evidence of syphilis so far as their physical well being is concerned are relatively good and the occasional patient who will develop a tertiary skin lesion does not justify treating every one of these patients.

DR. CHARLES R. REIN, New York: Drs. Crawford and Ray have again shown the importance of more sensitive serologic tests for the detection of syphilis. With the use of such tests they were able to detect cases of serologic syphilis which would have passed undiagnosed with the less sensitive tests. Recent serologic conferences held in the United States have demonstrated that there are at least five tests commonly used in this country which possess satisfactory specificity and adequate sensitivity. Dermatologists, however, should encourage the development and use of still more sensitive tests with satisfactory specificity by serologists. Such tests would detect more cases of so-called seronegative syphilis. The interpretation of the results obtained with such tests should be made by specialists.

DR. ARTHUR SCHOCH, Dallas, Texas: One word of criticism can be offered in spite of the fact that this is an excellent study: the serologic tests done in this particular study were based on comparatively few standard serologic tests. I mean the study as presented by the authors was based on the Hinton flocculation test and some Wassermann procedure. There are at least five standard serologic tests—the Kolmer Wassermann, the Hinton, the Kline, the Kahn and the Eagle. To base a study on two of the five and draw the conclusions that have been drawn seems specious. For the last few years we in Dallas who have been working with syphilis patients have used as a routine at

least three of these tests, and incidentally the technic is exactly as described by the originators, namely Kolmer, Kahn and Kline, and in the last two years we have added to that the Eagle complement fixation test and Eagle flocculation test. Now our routine procedure is to do not two or three serodiagnostic tests on the blood but five in parallel. This has taught us a few things. It has taught us much about the relative sensitivity of these various tests. It has taught us something about false positive tests in what we think are apparently normal individuals. I am talking from the standpoint of the clinician and not from the standpoint of the serodiagnostician. At the serologic conference in Hot Springs last fall the clinicians were in the minority. Here the laboratory diagnosticians are in the minority. So I think it is a matter of one's point of view as to whether we regard group C, D and E the authors had on slide 1 in the doubtful group, or whether we include just group D and E. Group C was the group in which the diagnosis of syphilis was made solely on a positive Hinton test or a very sensitive flocculation test for syphilis. It will take observation over a long period of years to determine whether group C, as the authors presented it, did have syphilis or did not. The group of individuals that Dr. Ryan spoke about indicating that it all depends on how sensitive a serologic test is as to whether or not it has prognostic import, with special reference to early syphilis, I think can be placed to one side. We have dark field examination to help us there make a definite diagnosis. The important group to consider is not the early syphilitic patient who is beginning to go into serologic positivity, but the enormous group that Dr. Lane spoke of. In my experience it is at least 60 per cent of our entire clinic clientele, and in the last two years we have thoroughly examined, not merely serologically and cursorily speaking from a clinical standpoint, 5,400 new patients with syphilis.

DR. G. MARSHALL CRAWFORD, Boston: Thank you for this generous discussion. Dr. Lane brought out two points that I didn't have time to emphasize: the matter of having several tests to establish the diagnosis and also to use different laboratories. I am also indebted to Dr. Kulchar for mentioning the reagin-like substance. I covered that in one sentence, saying that some men believe there is a substance which will occasionally show positives by certain tests. The elaboration by Dr. Kulchar was quite enlightening. I should like to repeat that the observation of these cases extended over a period of nine to ten months, so that temporary causes of an increase in their reagin-like substance should be eliminated. Whether a positive Hinton reaction means activity of syphilis and whether these patients should be treated were points I expected to see raised and was glad to hear. We do not feel that all these patients should be given intensive therapy. It has been our policy to treat only definitely active syphilis intensively and the others on an intermittent plan. Some very notable observers say that the human mechanism is not capable of conquering the syphilitic infection without help. We usually give them a short course once or twice a year. The hazards of the complement fixation test were also mentioned; they are largely avoided by the flocculation or precipitation test. I was glad to hear Dr. Rein mention the possibility that there is no seronegative stage. As long as there is some reagin present there must be something going on to produce that reagin. Dr. Rein may be forecasting the day when we shall simply make a diagnosis of syphilis and disregard stages except for infectiousness. Dr. Schoch's comments were very apropos. We are envious of him, having five serologic tests at his command. We do a routine Hinton and when that is positive always do a Wassermann; when there is a question we get as many checks as possible in another laboratory. While we don't think that some of our conclusions are far fetched on a few tests, they certainly could be improved if we had more. I should like to quote a few figures, as yet unpublished, from the last Serologic Congress. The Hinton test was done by five laboratories and there was not a single false positive or false doubtful from any of the five laboratories. There was no other test showing a complete absence of false positives. The Hinton test was 83.9 per cent sensitive on known positive specimens. The Kline exclusion test was close to that and the other five tests submitted to that congress were grouped in the 70's of percentage.

ACUTE PERFORATIVE DIVERTICULITIS OF THE COLON IN YOUNG PERSONS

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Based on reports of unselected postmortem examination [1] and on x-ray studies of the gastrointestinal tract of patients with abdominal symptoms,[2] the incidence of diverticulosis of the colon averages about 5.9 per cent. The average incidence under the age of 30 years is about 0.31 per cent of all diverticulosis patients; [3] therefore, the frequency of diverticulosis in persons under 30 years of age would be about 18 per hundred thousand of population.

In an average of about 15 per cent of patients with diverticulosis diverticulitis develops,[4] and approximately 21 per cent of these require surgical intervention,[5] or about 3 per cent of diverticulosis patients. For the entire population the incidence of operation would be about 186 cases per hundred thousand of population, and for persons under 30 years of age, diverticulitis requiring operation would occur in no more than 5.7 patients in 1,000,000 of population.

It is possible, however, that diverticulosis and diverticulitis occur more frequently in young adults than has been indicated by these reports. Postmortem studies do not portray the true incidence of diverticulosis in young persons, since there is only an approximate mortality of 0.4 per cent of the population who are under 30 years of age.[6] Likewise, the facts obtained from x-ray studies of the gastrointestinal tract are open to criticism. The average age of patients who have x-ray examinations made of the gastrointestinal tract has been given as 45 years.[2c] Diverticula may not be visible unless special efforts are made to demonstrate them, and repeated x-ray examinations of the gastrointestinal tract may be necessary. To ascertain the approximately correct incidence of diverticulosis in persons under 30 it would be necessary to have x-ray studies of the gastrointestinal tract made for diverticula of all persons during their first three decades of life.

Furthermore, Judd and Pollock [7] reported that of 118 operations for diverticulitis two, or 1.7 per cent, were performed on patients under 30 years of age. Also, in the course of my own private practice I have operated on three young adults for perforated diverticulitis with abscess, two of these patients being operated on within a period of two years.

1. (*a*) Koncour, E. J.: Colon Diverticula, Am. J. Surg. **37**: 433 (Sept.) 1937. (*b*) Rankin, F. W., and Brown, P. W.: Diverticulitis of the Colon, Surg., Gynec. & Obst. **50**: 836 (May) 1930.

2. (*a*) Mayo, W. J.: Diverticula of the Sigmoid, Ann. Surg. **92**: 739 (Oct.) 1930. (*b*) David, V. C.: Diverticulosis and Diverticulitis with Particular Reference to the Development of Diverticula of the Colon, Surg., Gynec. & Obst. **56**: 375 (Feb., No. 2A) 1933. (*c*) Spriggs, E. I., and Marxer, O. A.: Multiple Diverticula of the Colon, Lancet **1**: 1067 (May 21) 1927. (*d*) Rankin and Brown.[1b]

3. (*a*) Brown, P. W., and Marcley, D. M.: Prognosis of Diverticulitis and Diverticulosis of the Colon, J. A. M. A. **109**: 1328 (Oct. 23) 1937. (*b*) Spriggs and Marxer.[2c] (*c*) Rankin and Brown.[1b]

4. Abell, Irvin: The Diagnosis and Treatment of Diverticulitis and Diverticulosis, Surg., Gynec. & Obst. **60**: 370 (Feb., No. 2A) 1935. Mayo, W. J.: Diverticulitis of the Sigmoid, Brit. M. J. **2**: 574 (Sept. 28) 1929. Ochsner, H. C., and Bargen, J. A.: Diverticulosis of the Large Intestine; An Evaluation of Historical and Personal Observations, Ann. Int. Med. **9**: 282 (Sept.) 1935. Rankin and Brown [1b] and Marcley.[3a]

5. (*a*) Friedenwald, J., in discussion on Brown and Marcley.[3a] (*b*) Mayo.[2a] (*c*) Rankin and Brown.[1b]

6. Vital Statistics: Special Reports (Summary of the United States Registration Area, 1936), Dept. of Commerce, Bureau of the Census **4**: 957-958 (April 29) 1938. Estimated Population of the United States by Age as of April 1, 1935, ibid. Truesdell, L. E., Chief Statistician for Population, U. S. Dept. of Commerce, Bureau of the Census: Personal communication to the author.

7. Judd, E. S., and Pollock, L. W.: Diverticulitis of the Colon, Ann. Surg. **80**: 425 (Sept.) 1924.

REPORT OF CASES

CASE 1.—Mrs. J. P., aged 30, a housewife, admitted Jan. 21, 1925, had been taken ill five days previously with vomiting and constant abdominal pain, which was localized to the left lower quadrant. The patient was rather short and obese. The temperature was 102 F. There was considerable tenderness but no spasm in the left lower quadrant of the abdomen; no masses could be felt. Directions were given regarding the nonsurgical management of acute diverticulitis of the colon. Three days later the temperature was 102 F. and the pulse rate 120. An exquisitely tender mass the size of a large grapefruit was palpated for the first time in the left lower quadrant of the abdomen.

Operation was done the following morning. The mass consisted of omentum, adherent to the sigmoid, which was greatly thickened, particularly on the mesenteric border, and was covered with much fibrin. Associated with the mass was an abscess cavity containing about 8 ounces (240 cc.) of foul smelling pus. This was aspirated, and drainage was instituted. The patient made a satisfactory convalescence and was discharged from the hospital thirty days after operation. Gastrointestinal roentgenograms three and one-half months after the operation showed a diverticulum of the sigmoid.

CASE 2.—J. M., a man aged 23, admitted June 12, 1936, complained of intermittent abdominal pain of three weeks' duration which came on suddenly in the region of the umbilicus. He complained of diarrhea and vomiting on the day of the consultation as well as the day before. X-ray studies of the gastrointestinal tract showed moderate dilatation of several loops of small intestine; no diverticula of the colon were visible but the pattern of the mucosa seemed to be accentuated. A barium sulfate enema had been given and fluoroscopic examination showed tenderness at the junction of the descending colon and sigmoid. The patient was well developed and well nourished. The temperature was 99.6 F. Examination of the abdomen revealed exquisite tenderness and resistance at the left lower quadrant. Rectal examination disclosed a mass that could just be reached by the examining finger.

At operation a moderate amount of straw-colored fluid was found in the peritoneal cavity. The descending colon was adherent to the lateral parietal peritoneum, where there was a mass the size of a baseball. Within this mass was an abscess cavity from which about 4 ounces (120 cc.) of foul smelling pus was aspirated. A cigaret wick was placed into the cavity. The convalescence was fairly uneventful and the patient left the hospital on the thirty-seventh postoperative day. Roentgenograms of the gastrointestinal tract six months after the operation showed a diverticulum of the descending colon.

CASE 3.—Miss E. G., aged 19, a bookkeeper, admitted March 26, 1937, complained chiefly of abdominal pain, which after onset four days previously had localized to the right lower quadrant. Two days before admission she had an evening temperature of 101 F. There was no nausea and no vomiting. The patient was well developed and well nourished. The temperature was 100.5 F. Examination of the abdomen revealed tenderness, resistance and an indefinite fulness to the right of the umbilicus. Rectal examination was negative.

Operation revealed a mass the size of a tennis ball in the region of the ascending colon. Within the mass was an abscess cavity from which about 1 ounce (30 cc.) of thick, foul smelling pus was aspirated. A cigaret wick was placed into the cavity. The convalescence was relatively uneventful, and the patient was discharged from the hospital three weeks later. Roentgenograms of the gastrointestinal tract ten months after the operation showed a diverticulum of the ascending colon.

COMMENT

The causation of diverticulosis is still obscure. Although various explanations have been offered for the development of diverticulosis, such as old age, constipation with increased gaseous pressure within the colon, excessive fat or emaciation, and even a disturbance of the sympathetic nerves of the colon,[2a] it seems that the most applicable cause in young persons is an inherent weakness in the structure of the colon, which is usually at the point of entrance or exit of the blood vessels.[8] The possibility of diverticula being congenital should also be considered, since cases have been reported in children and even in infants.[9]

In young adults, as in older patients, diverticula rarely give rise to symptoms until there are inflammatory changes. These changes may be brought about by trauma,[10] such as repeated straining at stool, enemas given at high pressure, the use of drastic cathartics, and strenuous exercise. Food may also be a factor in causing diverticulitis;[2a] red meats, for instance, may increase the bacterial activity within the intestine, and potatoes and milk may cause irritation by forming a relatively large mass. The possibility of an infection from a distant focus[11] should also be considered.

In diverticulitis the symptoms may closely resemble those of acute appendicitis. Pain, the outstanding symptom, may vary in intensity and may be intermittent or constant. Nausea and vomiting may be present. There is always localized abdominal tenderness and at times rigidity as well as distention. The temperature is usually elevated and there is an accompanying leukocytosis.

When diverticulitis involves the ascending colon, as in case 3, the diagnosis may be confused with an appendical abscess until the abdomen is opened. If, however, the lesion is on the left side a correct preoperative diagnosis is frequently made. At times an abscess associated with diverticulitis can be felt by rectum. Fluoroscopic and sigmoidoscopic examinations may be of help in making an accurate diagnosis but are not without risk; if too vigorous, rupture of the abscess may result.

In early diverticulitis, that is, before perforation and abscess formation, inflammation may subside under nonsurgical management. This treatment should consist of rest in bed, practically nothing by mouth for a day or two, and ice bags or heat to the seat of pain. The heat may include short wave diathermy, electric pads, hot packs, Elliott treatment or rectal irrigation of warm physiologic solution of sodium chloride or olive oil. After the inflammation begins to subside, olive oil (2 or 3 ounces) or liquid petrolatum may be given by mouth, and later food, the diet at first being practically free of residue. Subsequently the patient should be put on an anticonstipation diet and given oil or agar by mouth.

If an abscess is present when the patient is first seen, as in the cases reported, or if in spite of medical treatment perforation and abscess formation take place, operation for the drainage of the abscess is indicated. If obstruction is present, cecostomy should also be done and, if the obstruction persists after the acute inflammation has subsided, resection of the obstructed area may be necessary.

Following recovery from an operation for perforated diverticulitis, the patient should be advised that

8. Hansemann and Klebs, cited by Judd and Pollock[7] and by David.[3b] Rankin and Brown.[1b] Judd and Pollock.[7] David.[3b]

9. Hartwell, J. A., and Cecil, R. L.: Intestinal Diverticula, Am. J. M. Sc. **140**: 174, 1910. Ashhurst, A. P. C.: Sigmoid Diverticulitis (Mesosigmoiditis) in a Child, Ann. Surg. **47**: 300, 1908. Ransohoff, J.: Acute Perforating Sigmoiditis in Children, Ann. Surg. **58**: 218, 1913. Goebel, cited by Ransohoff. Erdmann, J. F.: Acute Diverticulitis of the Colon, New York State J. Med. **109**: 969 (June 7) 1919. Judd and Pollock.[7]

10. Telling, W. H.: Acquired Diverticula of the Sigmoid Flexure, Lancet **1**: 843, 1908; Multiple Diverticula of the Sigmoid Flexure, Brit. M. J. **2**: 1346, 1908.

11. Rogers, J. T.: Diverticulitis of the Colon, Minnesota Med. **6**: 35 (Jan.) 1923. Spriggs and Marxer.[2c]

diverticulosis is still present. In order to avoid further development of diverticula or a recurrent diverticulitis, large doses of kaolin,[5a] bismuth subnitrate or barium sulfate [12] once or twice a week may be helpful. Particular attention should be given to regularity at stool; agar may be taken for bulk and soft stools.[3a] An effort should be made to improve the intestinal flora.[2b] It would be well for the patient to exclude from the diet coarse and indigestible foods and to include cooked fruits and finely chopped vegetables.[3a]

SUMMARY

1. Diverticulosis and diverticulitis of the colon probably occur more frequently in young persons than reports would indicate.

2. In this report young adults required operation for perforated diverticulitis of the colon with abscess.

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EPIDEMIC ENCEPHALITIS IN NORTH DAKOTA

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During July, August, September and October 1938 an epidemic of acute encephalitis, which clinically resembled the St. Louis type, was observed in North Dakota. According to information supplied by Dr. John Cowan, of the North Dakota Department of Health, 101 instances were reported, of which fifty-two occurred in Minot and the surrounding rural territory, which includes the ten counties in the northwestern portion of the state. Twenty-three of these patients were cared for in Trinity Hospital by the members of the medical staff, and the material of this report was obtained from their clinical records. Nine entered the hospital from Minot, while fourteen came from farm homes located within a radius of 65 miles of the city. The rural patients lived from 10 to 120 miles apart, and in only two instances did more than one patient come from any single locality.

Nineteen patients were adults and four were children. Arranged according to age groups, the incidence among adults was evenly distributed from 20 to 70 years. Nine of the adults were men and ten were women. The four children ranged from 2 months to 8 years in age. Two were boys and two were girls. Most of the city patients were engaged in business or professional pursuits, and one was a nurse who had cared for patients ill with encephalitis. The severity of the symptoms was not related to age and was just as marked in the younger as in the older patients. Five died of the illness and were respectively 25, 26, 36, 57 and 60 years of age.

The illness was characterized by an acute onset with generalized severe headache and fever. The temperature when first taken at home ranged from 101 to 105 F., the average being about 102 F. The commonly used analgesics gave no relief from headache. The patients complained of severe generalized muscular pains and backache. Chills and chilly sensations occurred when the temperature elevation was marked. Nausea and vomiting occurred in about one half of the patients early in the illness. Dizziness and drowsiness appeared within the first three days, but in spite of the drowsiness the patients were unable to sleep. After the fourth day, coarse or fine muscular tremors of the arms and face were present in about three fourths of the adult patients. The tremors were of the intention type and were absent at rest.

The symptoms of individual patients varied considerably. One became comatose on the first day of the illness while the mental symptoms of ten others did not progress to a state of delirium. Eight of the adult patients became irrational and delirious on the fourth or fifth day, and this condition was followed by coma within two days of all but one of these patients. For a time they could be aroused momentarily to take food, but later coma became deeper and incontinence of urine and feces occurred. Coma was a grave prognostic sign and five of the eight comatose patients died, four within two days after the onset of coma and one after eleven days.. Two of the five had repeated convulsions before death and one had a right hemiplegia which could not be explained by cerebral hemorrhage or thrombosis at the postmortem examination. A third patient died of paralysis of the respiratory center, the respirations gradually slowing to 4 or 5 a minute. In only one instance was there a terminal bronchopneumonia.

In the children the onset was sudden with high fever. Vomiting, nervous irritability and convulsions were the most frequent symptoms, while coma of only one patient occurred. Spasmodic muscular contractions of the right arm and leg of one infant were noted. Recovery of children was rapid, and the course of the illness was several days shorter than that of adults.

Most of the patients had been ill three or four days before admission to the hospital. Physical examination disclosed no constant changes in the heart, lungs or abdomen. Rigidity of the neck, the most characteristic physical finding, appeared early in the illness and was present in fifteen cases. This sign was elicited by any passive effort to bring the head forward on the chest. Coarse intention tremors of the hands and face, particularly of the lips, were observed in all but seven cases, and in four there was slurred speech, apparently related to the tremor of the lips and tongue. The abdominal reflexes were absent in ten instances and later became absent in two more. The Kernig sign was positive in six of the cases in which there was rigidity of the neck. The Babinski reflexes were positive in only four cases and varied from time to time. There were no characteristic abnormalities of the patellar and achilles tendon reflexes. Lateral nystagmus was present in two cases, and in two others a fixation nystagmus was demonstrated. In one of the latter there was a transient divergent squint.

The temperatures on admission to the hospital ranged from 100.6 to 105.6 F., most of them being between 102 and 104 F. In those cases in which recovery occurred the temperature remained elevated from three to seven days after the onset and then subsided to normal within two or three days. The average duration of fever was about eight days. The pulse and respiratory rates were increased proportionately to the temperature.

Recovery from delirium, somnolence, muscular tremor and rigidity of the neck were complete within

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From the Medical Service and Laboratory of Trinity Hospital and the Northwest Clinic.

one week after the temperature became normal. In one instance muscular tremor persisted for about six weeks. The average duration of the illness before convalescence was well established was fifteen days.

LABORATORY EXAMINATIONS

The average white blood cell count was 12,200, the lowest being 5,200 and the highest 22,700. The differential blood counts disclosed no constant change.

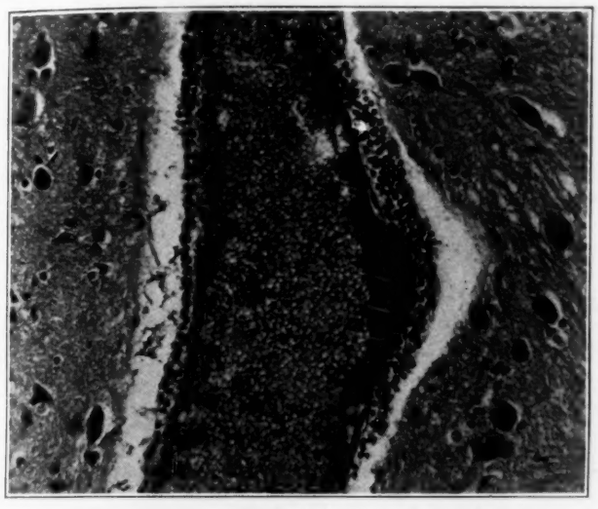

Fig. 1.—High power microscopic field demonstrating perivascular round cell infiltration.

Examination of the urine revealed albuminuria in eleven instances, the amount varying from 10 to 800 mg. per hundred cubic centimeters, but in most cases it was not more than 50 mg. per hundred cubic centimeters. Two patients showed traces of dextrose in the urine, and a third showed a large amount of dextrose with acetone and diacetic acid. This patient's blood sugar was 240 mg. per hundred cubic centimeters and death occurred on the ninth day of illness, although hyperglycemia and glycosuria were controlled by insulin.

In one fatal instance, the blood culture was repeatedly positive for the hemolytic streptococcus, and in four cases in which typhoid was suspected the Widal test was negative.

The average white cell count of the spinal fluid was 130, and it varied from 2 to 525 cells in individual instances. In adults about 80 per cent of the cells were lymphocytes and the rest polymorphonuclear leukocytes, while in children about 50 per cent of the cells were polymorphonuclear leukocytes. The spinal fluid sugar content, not including that of the diabetic patient, ranged from 45 to 104 mg. per hundred cubic centimeters, the average concentration being 72 mg. per hundred cubic centimeters. The cerebrospinal fluid pressure with the patient lying on the side ranged from 100 to 230 mm. of spinal fluid. The Nonne test was faintly positive in seven cases, and Lange's colloidal gold test was negative in five. The spinal fluid was cultured in seven instances and found sterile.

PATHOLOGY

Postmortem examination was performed on all five patients who died. The characteristic pathologic changes were limited to the central nervous system, and examination of the thoracic and abdominal tissues disclosed only such changes as might have been found in any severe toxic illness. When the dura was reflected from the brains a marked hyperemia of the leptomeninges was the most noteworthy change. There was some flattening of the cerebral convolutions and narrowing of the sulci, and on surfaces made by cutting, the tissue of the brains was pink.

Histologically the leptomeninges were diffusely infiltrated with lymphocytes, although plasma cells and epithelioid cells were occasionally seen. The infiltration was most marked over the base of the brain, while over the vertex the cellular exudate was most abundant opposite the cerebral sulci. The small blood vessels of the brain and of the leptomeninges were widely distended with erythrocytes. Thrombi were found in a few small arteries in the basal ganglions of one brain and were associated with small recent hemorrhages in the surrounding tissue.

The most striking microscopic change was a marked perivascular round cell infiltration. This occurred in all parts of the brain but was less marked in the cerebral cortex and medulla than in the basal ganglions, pons and medulla oblongata. Occasional lesions were found in the cerebellum. The round cell exudates occupied the so-called Virchow-Robin spaces and only rarely were round cells found between the blood vessels and the brain substance. The cells were chiefly lymphocytes but plasma cells, epithelioid cells and polymorphonuclear leukocytes were occasionally identified.

A second characteristic change consisted of aggregates of mononuclear cells widely distributed in the gray and white matter of the brain. These lesions varied in size but ordinarily were not more than 250 microns in the greatest diameter. The mononuclear cells were apparently of glial origin. Their nuclei were rather large, round or oval, and often indented. The cytoplasm was scanty, irregular in outline and poorly defined. In the larger cell aggregates occasional lymphocytes were identified. The cell masses were not related to the vascular lesions and occurred independently of them.

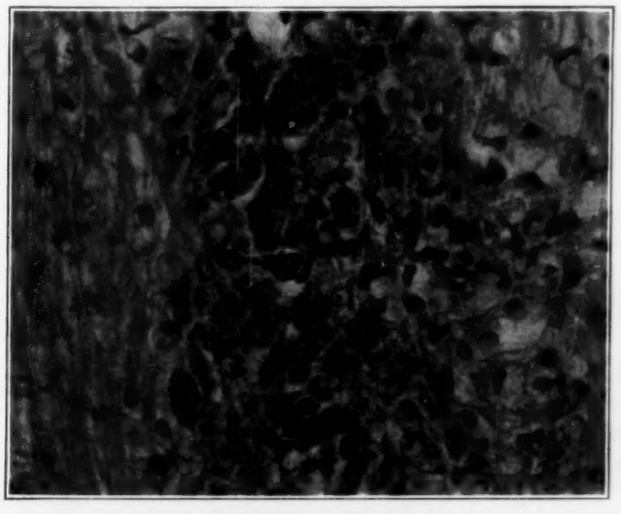

Fig. 2.—High power microscopic field from region of glial proliferation.

In all five brains degenerative changes of the large nerve cells were observed in the basal ganglions and pons, medulla oblongata and occasionally the cerebral cortex. The changes consisted of swelling and rounding off of the cell bodies with disappearance of the Nissl granules. The nuclei of these cells stained more deeply than normal, and the nuclear outlines were indistinct. In some no nuclear substance was visible and the rounded or irregular cell remnants were stained deep pink in hematoxylin and eosin preparations. Such cell

remnants were most frequently found in or near the regions of glial cell proliferation but were also found in the more normal tissue.

An unusual feature of the histologic preparations from the basal ganglions, pons and medulla oblongata was the presence of foci of demyelinization in which the normal brain tissue was replaced by a pale staining spongy fibrillar mass. These lesions were no larger than a miliary tubercle. Many of them were densely infiltrated with mononuclear cells similar to those found in the regions of glial proliferation, but it was not unusual to find foci containing almost no mononuclear cells. The lesions were irregularly distributed in the tissue. Some were arranged along the course of the blood vessels, but others occurred as isolated lesions unrelated to the blood vessels. Foci of demyelinization were not observed in the medulla or cortex of the cerebrum or cerebellum. The lesions were found in all five brains but the frequency with which they occurred varied considerably. They were numerous in three, while in the other two many microscopic sections were carefully examined before the lesions were demonstrated.

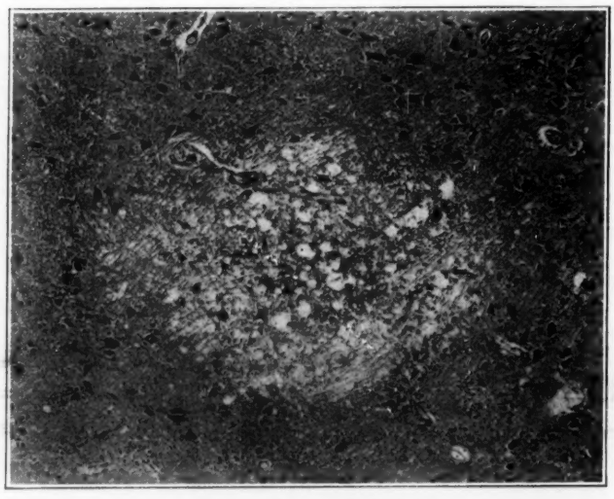

Fig. 3.—Low power microscopic field from lentiform nucleus, demonstrating region of demyelinization.

In three brains marked glial proliferation, perivascular round cell infiltration and degenerative changes in the nerve cells were noted in the olfactory bulbs.

Serums from six patients who recovered were examined in two laboratories. Dr. Edwin H. Lennette, of the Department of Pathology of Washington University School of Medicine, St. Louis, reported that four of the serums failed to neutralize the virus of Western equine encephalomyelitis or of lymphocytic choriomeningitis. Three of the four failed to neutralize the St. Louis encephalitis virus, while the fourth on repeated tests gave equivocal results.

Serums from the same four patients in addition to two others were examined in the laboratories of the National Institute of Health, of the U. S. Public Health Service in Washington, D. C., and Dr. Charles Armstrong was kind enough to report that in only one instance were neutralization tests with St. Louis encephalitis virus strongly positive. This serum was from the same patient in whom equivocal results had earlier been obtained by Dr. Lennette. Serum from four of these six patients was found to contain neutralizing antibodies against the Western virus of equine encephalomyelitis.

COMMENT

Acute epidemic encephalitis, as it was observed in North Dakota in the summer of 1938, resembled that reported in the St. Louis region in 1933.[1] The symptoms, physical manifestations and clinical course were similar. The seasonal incidence and the distribution of the cases in the community were much the same.[2]

The pathologic changes in the central nervous system, however, differed from those occurring in the St. Louis patients [3] in that small regions of demyelinization were found in the basal ganglions, pons and medulla oblongata. Because of the difference in the pathologic condition it was suspected that the illness in North Dakota patients might be caused by a virus different from that responsible for the St. Louis epidemic. As already stated, the serum from only one of six patients who recovered neutralized St. Louis encephalitis virus.

In view of the fact that encephalitis in human beings has been reported as caused by the virus of both Eastern and Western equine encephalomyelitis,[4] it is interesting to note that Western equine encephalomyelitis was prevalent in North Dakota in the summer of 1938. Serums from six of our patients who recovered were tested against the Western virus of equine encephalomyelitis, and Dr. Armstrong reported that the neutralizing antibodies were moderately positive in two instances and positive in two others.

The mortality in our series of patients was about 22 per cent. This figure is probably too high, since only seriously ill patients were brought to the hospital. The incidence of less severe acute encephalitis in the community could not be determined. The increased severity in the older age groups noted in St. Louis was not apparent in our patients.

In children the illness was first thought to be acute anterior poliomyelitis without paralysis, but later, because of the marked similarity of the clinical course to that in adults, the diagnosis was changed to acute encephalitis. Since all the children recovered, the pathologic changes could not be investigated.

SUMMARY

Twenty-three instances of acute epidemic encephalitis not previously observed occurred in North Dakota.

Clinically the illness resembled the St. Louis type of acute encephalitis.

Pathologically the North Dakota encephalitis differed from the St. Louis type in that foci of demyelinization occurred in the basal ganglions, pons and medulla oblongata.

Serum from only one of six patients who recovered neutralized the virus of St. Louis encephalitis, while serum from four of these six patients neutralized the Western equine encephalomyelitis virus. The virus of lymphocytic choriomeningitis was not neutralized by serum from these six patients.

The mortality in the reported series was 22 per cent.

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DESOXYCORTICOSTERONE ESTERS

CERTAIN EFFECTS IN THE TREATMENT OF ADDISON'S DISEASE

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During the past decade there have been two material advances in the treatment of patients suffering from Addison's disease. The first of these was the recognition of the abnormalities of electrolyte metabolism present in addisonian patients and the correction of these disturbances primarily through the addition of large amounts of sodium salts to the diet [1] and also through a reduction in the intake of potassium.[2] The second advance came through the elaboration of extracts of the adrenal cortex,[3] which are life sustaining, at least in adrenalectomized animals.

Despite the progress made through these contributions, the treatment of Addison's disease has continued to be only moderately satisfactory at best. In the past three years the isolation of a series of crystalline steroids of great physiologic activity from adrenal cortical material has been accomplished by Kendall,[4] by Wintersteiner and Pfiffner [5] and by Reichstein.[6] This work aroused the anticipation that one of these active steroids might be synthesized in sufficient amounts to make possible the treatment of adrenal insufficiency in man. This hope has been realized in the synthetic preparation of esters of desoxycorticosterone by Reichstein,[7] and the present report deals with the results obtained following their use in a series of thirteen patients with Addison's disease. These results are in general agreement with those reported by Thorn [8] and his associates and by Cleghorn and his colleagues.[9]

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Owing to lack of space, this arictle has been abbreviated for publication in THE JOURNAL by the omission of ten case reports. The complete article appears in the authors' reprints.

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9. Read before the American Society for Clinical Investigation, May 1, 1939.

EXPERIMENTAL

Observations were made of the effects of desoxycorticosterone esters [10] on various blood constituents including sodium, potassium, calcium, chloride, bicarbonate, nonprotein nitrogen, serum proteins, sugar and cholesterol. The effects on the excretion of water, sodium, potassium, total nitrogen and riboflavin were studied, and observations were made on changes in hematocrit, serum volume as measured with the blue dye method of Gregersen and Gibson, and total interstitial fluid volume as determined by the sodium thiocyanate method. Finally, in a number of instances the effects of desoxycorticosterone on the basal metabolic rate and carbohydrate metabolism were recorded.

In this study, six patients were placed on standard regimens in the metabolism service. Their diets were essentially constant as to the types and amounts of the various foodstuffs, caloric values and mineral content. These patients also received a constant fluid intake and

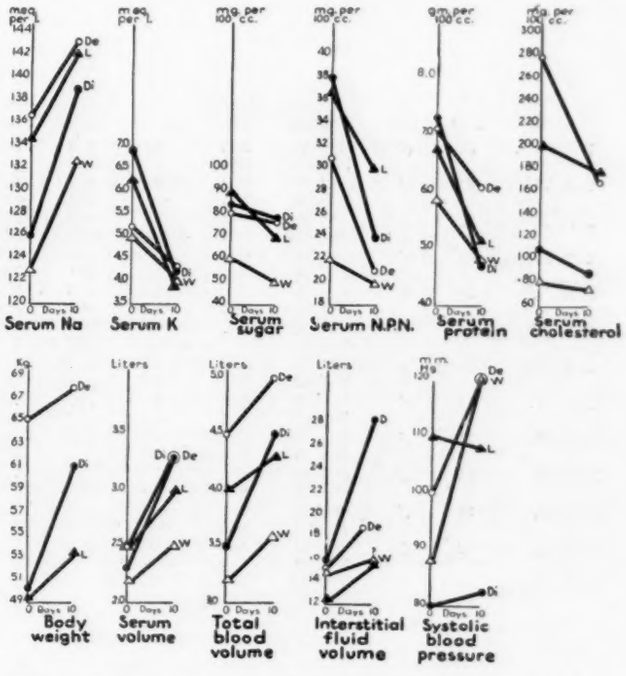

Fig. 1.—Summary of certain effects of desoxycorticosterone propionate observed after ten days' treatment of a group of patients with Addison's disease maintained on a standard regimen.

were given in addition to their food, which was prepared "salt free," a constant intake of sodium chloride. In addition to these rigidly controlled cases, observations were made on other addisonian patients who were allowed to eat and drink as they desired.

After a foreperiod of varying duration, the hospitalized patients received, as a rule, 25 mg. of desoxycorticosterone acetate or propionate daily for four days and then from 10 to 25 mg. daily for five days more. (The hormone, dissolved in sesame oil, was injected subcutaneously or intramuscularly once a day and each cubic centimeter contained 5 mg.) After this time the patients were allowed to eat as they desired and the dose of synthetic hormone was continued at a maintenance level. We have failed to detect any definite difference in activity between the acetate or propionate esters of desoxycorticosterone. The details of treatment are presented in the individual case histories.

10. The desoxycorticosterone esters used in this work were furnished by Roche-Organon, Inc. The term "doca" is employed as a contraction of the full chemical name.

RESULTS

The results are shown in part in the table and in figure 1 and can be summarized as follows:

Salt and Water Retention.—Desoxycorticosterone esters cause a striking retention of salt and water. The rate of retention of the sodium ion usually exceeds that of water, so that as a rule the serum sodium concentration increases to normal and is maintained at a normal level as fluid retention continues. In case 4 (fig. 2) water appeared to be retained more rapidly at first than the sodium ion, resulting in an actual decrease in the sodium level of the blood for three days. Following this the concentration rose to normal despite further water retention. In case 6, of extensive tuberculosis, it was never possible to raise the sodium concentration above 132 milliequivalents per liter although the retention of water was sufficient to cause pulmonary congestion, hydrothorax, generalized edema and a temporary elevation of venous pressure to 140 mm. of water.

The amount of salt and water retained varies greatly in different cases and cannot be correlated with the initial sodium or serum protein concentrations or with the initial plasma volumes. Patient 3 (fig. 3) gained 11 Kg. in ten days, during which time he received a total of 190 mg. of the hormone. In contrast, patient 1 gained but 2 Kg. in thirty days, during which time he received 725 mg. of hormone. Both of these patients received the same amounts of sodium and potassium salts in their diets.

Coincident with the retention of salt and water and gain in weight, there was in every case a considerable decrease in the urinary excretion of sodium, chloride and water. For example, in case 3 the urine output fell from an average of about 1,500 cc. daily to as little as 410 cc. during the period of administration of 15 mg. of hormone each day. The sodium excretion fell from the average control period level of 159 milliequivalents to as low a value as 28 milliequivalents in twenty-four hours and the chloride excretion underwent a comparable change.

As a result of these changes there were marked increases in the extracellular fluid volume in the various cases as measured by the sodium thiocyanate method. These increases were in general agreement with the gains in body weight except in case 1, in which repeated observations suggested an increase in extracellular fluid volume of 8.0 liters but a gain of only 3.3 Kg. in body weight. This discrepancy is not at present explainable. The data for salt and water retention in this case indicate that the validity of the thiocyanate figure is questionable.

The blood serum volumes increased between 0.3 and 1.2 liters during the first ten days of treatment in the six cases in which these measurements were made. These increases are in close agreement with the decreases in hematocrit and serum protein concentration and indicate that no significant change in red cell volume occurred.

No consistent alterations of albumin-globulin ratios occurred in the four cases in which this determination of the serum was made. These included the two cases in which the serum protein concentrations fell respectively from 7.3 to 4.7 and from 5.9 to 4.8 Gm. per hundred cubic centimeters.

Potassium Excretion. — Synthetic desoxycorticosterone esters cause a striking decrease in the concentration of potassium of the serum and frequently reduce it to abnormally low levels. Thus, in eight of nine cases the potassium concentration after treatment was lower than 4 milliequivalents per liter, the lower limit of our normal values. In no instance, however, did the potassium concentration fall below 2.9 milliequivalents per liter.

The urinary excretion of potassium increased on the first day of hormone injection in the six cases in which this was studied. Thereafter the potassium excretion was extremely variable. For example, in one case there

Summary of the Maximal Effects of the Administration of

Case	Age	Sex	Blood Pressure, Mm. Hg	Weight, Kg.	Edema	Interstitial Fluid Volume, Liters	Serum Volume, Liters	Hematocrit, per Cent Cells	Red Blood Cells, Millions	Serum Protein, Grams per 100 Cc.	Serum Albumin, Grams per 100 Cc.	Serum Globulin, Grams per 100 Cc.	Venous Pressure, Mm. H_2O	Vital Capacity, Cc.	Circulation* Time, Sec.	Serum Sodium, mEq. per Liter
1. S. McD.	35	♂	90/ 52	50.3	0	15.0	2.0	48.0	4.48	6.7	...	...	65	2,250	12	135.8
			142/ 86†	**53.3**	**0**	**23.0**	**3.0**	**32.0**	**4.00**	**5.7**			**75**	**2,450**	**13**	**140.8**
2. R. W.	47	♂	96/ 64	70.2	0	20.5	3.4	42.0	5.10	6.7	...	...	55	2,250	23	134.4
			146/108	**74.3**	**±**	**22.3**	**4.6**	**29.0**	**3.90**	**5.2**			**55**	**2,850**	**16**	**139.1**
3. M. D.	27	♂	78/ 50	50.1	0	15.9	2.3	36.0	4.71	7.2	4.4	2.8	80§	4,250§	..	126
			96/ 64	**64.4**	**++++**	**28.3**	**3.3**	**27.0**	**2.88**	**4.7**	**2.8**	**1.9**	**158**	**1.250**		**138.6**
4. F. D.	41	♂	96/ 58	66.8	0	15.1	2.5	44.5	3.70	7.1	...	...	...	.....	..	136.3
			120/ 85	**75.1**	**±**	**18.7**	**3.3**	**34.0**	**3.60**	**6.0**						**143.2**
5. M. L.	56	♀	100/ 68	50.2	0	12.6	2.5	42.0	3.85	6.6	...	...	...	.....	..	135.0
			160/ 92	**53.8**	**++**	**15.6**	**3.0**	**29.0**	**3.73**	**5.1**						**142.2**
6. H. W.	36	♂	80/ 52	....	0	14.7	2.2	31.0	3.80	6.5	3.9	2.6	75§	900§	..	122.4
			120/ 84		**++++**	**15.7**	**2.5**	**28.0**	**3.36**	**4.7**	**2.5**	**2.2**	**140**	**600**		**132.1**
7. M. C.	37	♀	100/ 70	45.4	0	....	...	....	....	6.2	4.2	2.0	...	.....	..	137.7
			118/ 80	**50.7**	**0**					**5.7**	**4.3**	**1.4**				**141.2**
8. A. W.	50	♂	100/ 80	55.4	0	....	...	....	4.48	6.8	4.8	2.0	...	.....	..	141.1
			104/ 65	**59.5**	**+**				**3.42**	**5.0**	**3.5**	**1.5**	**75**	**3,000**		**143.4**
9. H. B.	33	♂	100/ 72	60.8	0	....	...	....	4.84	7.0	...	...	...	.....	..	.....
			106/ 70	**62.1**	**0**				**4.70**	**5.9**						
10. A. G.	35	♂	105/ 65	51.1	0	....	...	....	....	7.4	...	...	...	.....	..	.....
			132/ 90	**55.5**	**++**					**6.5**						
11. R. F.	33	♂	94/ 70	61.1	0	....	...	....	....	7.0	...	...	...	.....	..	.....
			160/110	**63.8**	**++**					**6.0**			**250**			**143.5**
12. G. B.	52	♀	82/ 60	50.1	0	....	...	....	....	7.0	...	...	...	.....	..	.....
			132/ 88	**54.0**	**++**					**6.3**						
13. M. J.	43	♀	94/ 60	38.6	0	....	...	....	....	6.8	...	...	...	.....	..	.....
			90/ 60	**40.0**	**++**					**6.2**						

* Circulation time with 0.5 Gm. of calcium gluconate.
† Figures in bold face type are following desoxycorticosterone propionate or acetate and represent maximal effects.

resulted an increase in excretion of potassium far in excess of that which could be accounted for by a decrease in concentration in the interstitial fluid and also greatly in excess of that which might have been liberated by cell breakdown as judged by a slight increase in excretion of nitrogen. In another case the excess potassium excreted could be entirely accounted for on the basis of that lost from the interstitial fluid alone. In a third case the excess excretion was even less than might have been anticipated from the decrease in serum potassium level.

Nitrogen Excretion.—The nonprotein nitrogen level of the serum decreases even when it is within normal limits at the beginning of treatment.

Total nitrogen excretion may not be affected, but as a rule there is a slight increase not exceeding 2 Gm. in the first two or three days of treatment.

respiratory quotients measured before and after two weeks of hormone treatment in this case were 0.85 and 0.78 respectively—a change of questionable significance. In another case two hypoglycemic episodes occurred during which the blood sugar levels were 40 and 38 mg. per hundred cubic centimeters. This patient had been receiving 10 mg. of desoxycorticosterone daily for more than two weeks. This dose was insufficient to raise the blood sodium level above 122 milliequivalents per liter, although it was enough to cause excessive fluid retention.

Blood Pressure.—The effect of desoxycorticosterone derivatives on blood pressure is undeniable, although it does not appear as promptly as do the effects on salt and water metabolism. In all of the thirteen cases the blood pressure reached normal levels in the course of two to four weeks and in three cases it has risen gradu-

Desoxycorticosterone Esters Observed in Patients with Addison's Disease

Serum Chloride, mEq. per Liter	Serum Carbon Dioxide Content, mEq. per Liter	Serum Potassium, mEq. per Liter	Serum Calcium, Mg. per 100 Cc.	Serum Nonprotein Nitrogen, Mg. per 100 Cc.	Serum Dextrose, Mg. per 100 Cc.	Serum Cholesterol, Mg. per 100 Cc.	Basal Metabolic Rate, per Cent	Comment
99.5	27.6	5.0	10.0	29	72	172	—14	Gained only 3 Kg. in 3 weeks despite 25 mg. Doca‡ and 11.6 Gm. of salt daily
107.7	**26.5**	**3.7**	**9.1**	**22**	**81**	**151**	**—17**	
93.0	31.0	4.8	10.3	33	74	188	— 8	Gained only 3 Kg. in 12 days despite 25 mg. Doca and 7.9 Gm. of salt daily
103.0	**29.0**	**3.5**	**9.0**	**29**	**87**	**163**	**± 0**	
100.0	20.3	7.7	10.1	41	78	134	....	Gained 11 Kg. in 10 days with about 20 mg. of Doca daily; gained 0.5 Kg. regularly with 5 mg. of Doca without salt added to diet
106.7	**25.6**	**4.0**	**8.6**	**24**	**82**	**89**		
100.0	26.3	5.2	....	31	82	279	....	Gained 2.2 Kg. in 10 days on 20 mg. of Doca and 11.6 Gm. of salt daily
108.8	**27.0**	**3.9**		**21**	**77**	**168**		
100.0	22.4	6.3	....	38	78	212	....	Gained 3.7 Kg. in 10 days on 20 mg. of Doca and 6.6 Gm. of salt daily
109.4	**26**	**3.9**		**30**	**76**	**178**		
94.0	23	5.1	8.7	27	63	81	....	Died; marked hydrothorax and ascitic fluid; massive edema; extensive tuberculosis of adrenals, peritoneum and spine; had fever and ate poorly in last weeks
102.0	**27.2**	**3.9**	**8.0**	**17**	**35**	**66**		
108.0	22.5	3.9	10.1	23	70	195	....	Gained 3 Kg. in the hospital on 12.5 mg. of Doca and 10 Gm. of salt daily; maintained in office on 15 mg. of Doca every two days and 5 Gm. of salt daily
113.0	**25.7**	**3.6**	**8.9**	**23**	**71**	**165**		
106.0	25.6	4.7	10.0	25	85	143	....	In hospital, gained 4.5 Kg. in 10 days on 15 mg. of Doca and 10 Gm. of salt daily
112.0	**26.6**	**3.7**	**9.0**	**22**	**88**	**140**		
101.0	....	...	....	30	63	...	....	Patient treated in clinic; gave himself 12.5 mg. Doca every other day; taking 2 teaspoonfuls of salt daily
108.0				**21**	**80**			
98.8	....	...	....	27	71	...	....	Patient given 15 mg. of Doca daily for 2 weeks and then 12.5 mg. every other day; taking 5 Gm. of salt daily
105.3				**23**	**71**			
105.0	....	...	....	27	64	...	....	Patient treated in clinic; after 2 mo. on 15 mg. of Doca every other day and 10 Gm. of salt daily, he was admitted with marked congestive heart failure; died
109.0		**2.9**		**22**	**83**			
108.0	....	...	....	..	87	...	....	Patient treated in clinic; getting 15 mg. of Doca every other day and 10 Gm. of salt daily; 6 wk. after start she died suddenly at home; death was unexplained
108.4					**75**			
100.0	....	...	....	26	69	...	....	Treated at home with 15 mg. every 2 days and 8 Gm. of salt daily for 2 weeks; because of local reaction, Doca stopped for 2 weeks; last 3 weeks on 10 mg. of Doca every 2 days and 5 Gm. of salt daily
104.0				**22**	**81**			

§ After return to normal.
‡ Doca = Desoxycorticosterone acetate or propionate (Roche-Organon).

In the two cases in which determinations were made it appears that ammonia excretion increases within twenty-four hours after desoxycorticosterone has been administered.

Blood Calcium and Cholesterol.—The serum calcium concentration decreases following administration of the hormone. This was observed to be true in each of six cases in which determinations were made before and ten days after the initiation of treatment. This change may be attributed to hemodilution with its attendant decrease in serum albumin concentration.

The cholesterol content of the blood also decreases, probably as a result of hemodilution.

Carbohydrate Metabolism.—No evidence has been found to suggest that desoxycorticosterone esters have any effect on carbohydrate metabolism. The fasting blood sugar level is often as low or even lower after from ten to forty days of treatment. In case 1, in which 25 mg. of hormone was administered daily for thirty days, the fasting blood sugar level was 74 mg. and four hours after the ingestion of 100 Gm. of dextrose it was 46 mg. per hundred cubic centimeters. The

ally to 160/92, 160/110 and 146/108 respectively. It does not seem likely on the basis of the history that any of these patients suffered from hypertensive vascular disease before the onset of Addison's disease.

Miscellaneous Effects.—In addition to the objective changes described, all of the patients feel stronger and their characteristic early morning asthenia and nausea disappeared during the course of treatment with the synthetic hormone. No definite effect on pigmentation has been noted beyond that attributed to rehydration and no change in riboflavin excretion has been observed.

Effect of Progesterone.—In view of recent observations on the similarity of action of progesterone and desoxycorticosterone [11] in animals, their relative effects were compared in three cases of Addison's disease. The results in two of these are shown in figures 3 and 4. It is clear that the daily subcutaneous administration of

11. Thorn, G. W., and Engel, L. L.: The Effect of Sex Hormones on the Renal Excretion of Electrolytes, J. Exper. Med. **68:** 299 (Sept.) 1938. Gaunt, Robert; Nelson, W. O., and Loomis, Eleanor: Cortical Hormone-like Action of Progesterone and Noneffect of Sex Hormones on "Water Intoxication," Proc. Soc. Exper. Biol. & Med. **39:** 319 (Nov.) 1938. Greene, R. R.; Wells, J. A., and Ivy, A. C.: Progesterone Will Maintain Adrenalectomized Rats, ibid. **40:** 83 (Jan.) 1939.

progesterone in doses of 30 mg. given for seven or eight days was entirely without either subjective or objective effect. Whether larger doses might have had some effect is not known.

COMPLICATIONS

In view of the high degree of physiologic activity of desoxycorticosterone esters, it could be expected that overdosage might result in the appearance of disturbing complications. Indeed, ten of thirteen patients developed edema varying from mild and transient puffiness of the face and ankles to massive anasarca. Patients 3, 6 and 11 developed respiratory distress, tightness in the chest, a rise in venous pressure and a decrease in vital capacity associated with x-ray evidence of pulmonary congestion, as shown in the table. Patient 3 also developed striking dilatation of the right side of the heart (fig. 5). In this patient the rapid increase in blood volume from 3.6 liters up to 4.5 liters was associated with the development of hypoproteinemia, circulatory

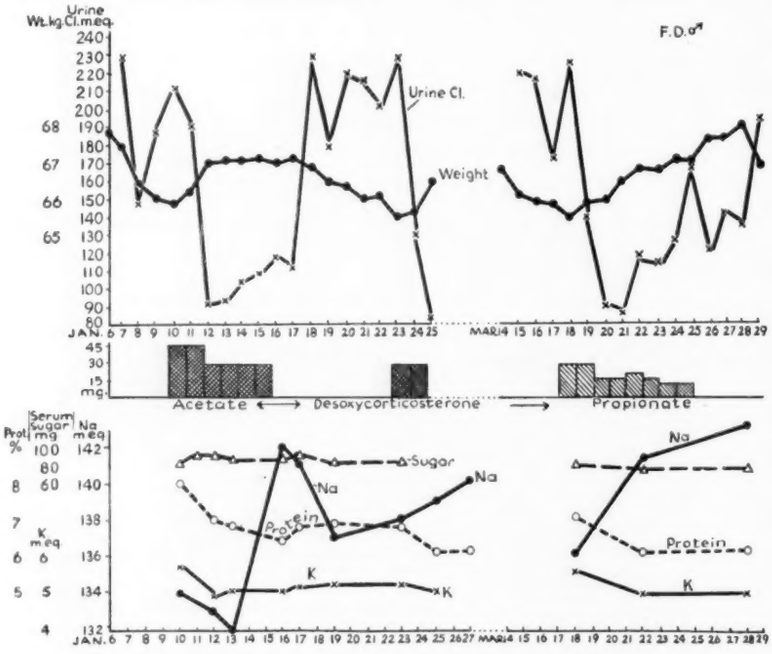

Fig. 2 (case 4).—Effects of desoxycorticosterone acetate and propionate.

embarrassment and edema. It was necessary to resort to the restriction of fluid and salt to do away with this "edema of adrenal origin." He improved promptly, and in the course of fourteen days his venous pressure dropped from 157 mm. to 80 mm. of water, his cardiac dilatation disappeared (fig. 6), his vital capacity rose from 1,250 cc. to 4,250 cc., and except for slight puffiness of his face and ankles his edema disappeared. It is of interest to note that after this improvement had taken place the circulating blood volume was still 4.5 liters.

In case 11, serious cardiac insufficiency associated with a rise in venous pressure to 250 mm. of water and a rise in arterial pressure to 160/110 mm. of mercury developed at a time when the patient was taking only 15 mg. of desoxycorticosterone every other day and from two to three teaspoonfuls of salt in his diet. The difference in the size of his heart before and after treatment may be seen in figures 7 and 8. Following phlebotomy and the limitation of salt and water the venous pressure fell but the patient succumbed with a terminal pneumonia. The details are described in the case record. Autopsy revealed no adequate organic basis for the dilatation of the heart, although mild hypertrophy was present.

The mechanism for the development of cardiac insufficiency in these three cases is not clear. A rapid and extensive increase in circulating blood volume is a possible factor, although in case 6 the increase in blood volume caused by the hormone was only 300 cc. at the time when the venous pressure was elevated and symptoms were most marked. The possibility of vitamin B_1 deficiency as an etiologic factor has been considered but, with the exception of relatively low excretion of thiamin in the urine, we have no evidence to support this idea.

REPORT OF CASES

CASE 3.—*History.*—M. D., a man aged 27, unmarried, a soda clerk, whose history prior to the present illness contained no significant facts, for about ten years had tanned easily and noticed that the tan did not fade normally. One year before admission he consulted a physician because of weakness, anemia (hemoglobin 75 per cent, erythrocytes 3,700,000) and he improved following treatment. The present illness was finally precipitated by a reaction to tetanus antitoxin given for a hand injury; after considerable vomiting he received a saline infusion with spectacular benefit and the diagnosis of Addison's disease was made. In spite of the use of salt and small amounts of adrenal cortex extract he continued to fail and a perirectal abscess accelerated this trend. He lost 19 pounds (8.6 Kg.) in the four months before coming to the Presbyterian Hospital. On admission he was thin, markedly pigmented both in skin and mucous membranes, and obviously ill; the blood pressure was 80 systolic, 40 diastolic, and there was acrocyanosis and a fistula in ano. There was no evidence of tuberculosis. His sedimentation rate on admission was 68 mm. in one hour, but he was afebrile. The basal metabolism was —8 on February 27. Chemical studies on admission showed the serum sodium 126 milliequivalents per liter, potassium 7.7 milliequivalents per liter, blood sugar 78 mg. per hundred cubic centimeters and nonprotein nitrogen 41 mg. per hundred cubic centimeters.

This was a typical case of Addison's disease, probably due to atrophy of the adrenals and complicated by a rectal fistula.

Treatment with Desoxycorticosterone.—The patient was placed on a constant diet with measured and constant intake of sodium (12.3 Gm.), potassium and water. He was then given 30 mg. of progesterone daily intramuscularly for eight days and no demonstrable effect was noted on weight, blood pressure, excretion of urine chloride or in serum electrolytes. He was then given 25 mg. of desoxycorticosterone subcutaneously for four days. His weight increased 1.7 Kg., the urine volume was halved and there was no marked change in urinary nitrogen. Urine chloride excretion was decreased 30 per cent, sodium excretion 60 per cent, and urine potassium excretion was increased about 60 per cent. Serum cholesterol decreased from 112 to 102 mg. per hundred cubic centimeters, serum sodium rose from 126 to 132 milliequivalents per liter, chloride from 100 to 104 milliequivalents per liter, bicarbonate from 20 to 23 milliequivalents per liter, serum potassium fell from 6.9 to 4.3 milliequivalents per liter, protein 7.3 to 5.6 per hundred cubic centimeters, nonprotein nitrogen from 38 to 30 mg. per hundred cubic centimeters. The serum sugar was not changed. The extracellular fluid volume rose from 15.9 to 19.8 liters. The hematocrit reading fell from 34 to 27.5 per cent cells. The blood pressure was not altered. The patient was then given between 10 and 15 mg. of desoxycorticosterone subcutaneously daily for the next seven days and gained 9.1 Kg. more weight. At this time there was marked edema of the face, sacrum and ankles. The venous pressure was elevated (158 mm. water), the vital capacity was lowered to 1,250 cc. and he had developed an acute dilatation of the right side of

the heart (fig. 5). During this period the urine output was about one half of that in the foreperiod. The excretion of urine chloride varied but was usually below that of the foreperiod by about 45 per cent. Excretion of urine sodium was 30 per cent of that during the foreperiod and urinary potassium was about 20 per cent less than during the foreperiod. His serum sodium had risen to 138.6 milliequivalents per liter from 131.6, chloride to 107 milliequivalents per liter from 104, bicarbonate to 25.6 from 23.1 milliequivalents per liter. The serum potassium remained about the same after the first four days and at this time was 4.2 milliequivalents per liter. The serum

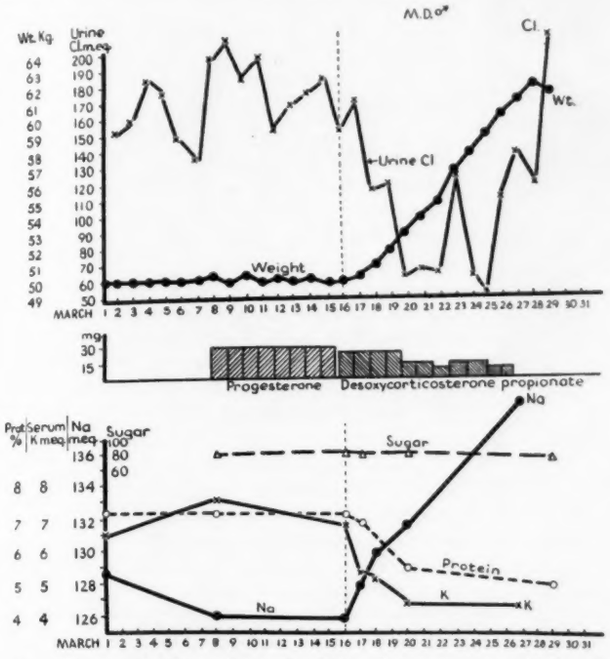

Fig. 3 (case 3).—Comparison of effects of progesterone and desoxycorticosterone propionate.

protein continued to fall from 5.6 to 4.7 per hundred cubic centimeters, the nonprotein nitrogen fell to 24 mg. per hundred cubic centimeters from 30, and the serum sugar continued to remain the same. The serum volume had risen to 3.3 liters from 2.3 liters at the start of the administration of desoxycorticosterone. The extracellular fluid volume had risen from 15.9 at the start to 28.3 liters. The blood pressure remained about the same. The serum cholesterol had fallen to 89 mg. per hundred cubic centimeters from 102. The restriction of salt and water for three days was necessary to stop progressive gain in edema and cardiac insufficiency. Thereafter the patient was on an unlimited diet and fluid intake. Salt was restricted somewhat and he was given 5 mg. of desoxycorticosterone every two to three days. He gradually lost his edema, his venous pressure and vital capacity returned to normal, his cardiac dilatation disappeared (fig. 6) and about six weeks after the first injection of desoxycorticosterone he had gained 14 Kg. and had no edema. His serum sodium remained about 135.5 milliequivalents per liter, potassium 4 milliequivalents per liter, the serum protein had risen to 6.6 per hundred cubic centimeters and the serum cholesterol to 134 mg. per hundred cubic centimeters. The extracellular fluid volume was 25.5 liters and the blood volume 4.6 liters as against 28.3 and 4.5 liters respectively at the height of his edema. At this time his blood pressure had risen about 15 mm. of mercury systolic but the diastolic had not changed and he still had a blood pressure consistently under 100. His general clinical status was as different from his original condition as possible and he felt perfectly well up and around. He was given a constant diet again for a six day period and given 25 mg. of desoxycorticosterone by mouth for three days. This was five times the amount needed to maintain him when given subcutaneously and had no effect on his chloride excretion or on his serum values. He lost weight and the serum potassium rose from 4.4 to 5.4 milliequivalents per liter on this regimen. He was returned to his former regimen of desoxycorticosterone 5 mg. every two to three days and a regular diet with no added salt and had the fistula in ano repaired. He was under general anesthesia for an hour and withstood the operation uneventfully with only one saline infusion postoperatively. He is now still in the hospital, recovering from his operation, and two and one-half months after the start of desoxycorticosterone administration he has gained a total of 14 Kg. and has maintained his serum electrolyte values at nearly normal levels on 5 mg. of desoxycorticosterone every three days. More than this leads to edema. His blood pressure after ten weeks of desoxycorticosterone remains below 100. A dextrose tolerance curve done two months after the start showed a flat curve but no hypoglycemia four hours after ingestion of 100 Gm. of dextrose.

CASE 4.—*History.*—F. D., a man aged 41, married, an editor, had a nervous breakdown in 1920 and progressive leukodermia since 1921. In 1936 he noticed that his summer tan did not fade in the winter. Beginning in August 1937 he suffered from increasing weakness, anorexia and loss of weight (20 pounds, 9 Kg.) in all. On admission his blood pressure was 70 systolic, 60 diastolic, and his nonleukodermic skin was pigmented but there was no pigmentation of the mucous membranes. The blood count and urine were normal; the sedimentation rate was 20 mm. in one hour. Roentgenograms of the chest and adrenal areas were negative. The serum sodium was 127.7 milliequivalents per liter, potassium 5.6 milliequivalents per liter, the blood sugar 96 mg. per hundred cubic centimeters and the nonprotein nitrogen 47 mg. per hundred cubic centimeters.

On salt administration he improved greatly and the addition of cortical extract made little if any difference. He was followed in the hospital and clinic until Jan. 5, 1939, when he was readmitted for desoxycorticosterone administration. During this time he was able to work at intervals, his serum sodium remaining normal most of the time but his blood pressure usually being below 100 systolic.

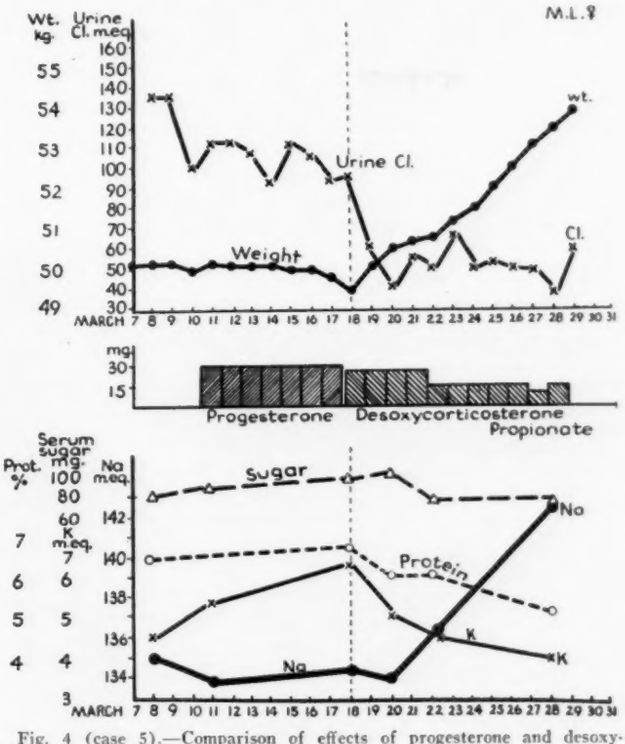

Fig. 4 (case 5).—Comparison of effects of progesterone and desoxycorticosterone propionate.

A man of 40 with Addison's disease greatly helped by salt administration but never returning to normal strength, his emotional make-up interfered with an accurate appraisal of his condition at times. There was no evidence of tuberculosis. Leukodermia was a coexisting condition.

Treatment with Desoxycorticosterone.—The patient was placed on a constant diet containing known amounts of sodium chloride (11.6 Gm.), potassium and water. He was then given 25 mg. of desoxycorticosterone intramuscularly daily for four days and gained 1 Kg. in weight. The urine volume was decreased by

about 10 per cent, the urine chloride by 50 per cent, the urine sodium by 70 per cent. The urine nitrogen was increased by about 10 per cent and the potassium by about 50 per cent. The serum sodium rose from 136.3 to 141.6 milliequivalents per liter, chloride from 100 to 104.8 milliequivalents per liter, bicarbonate from 26.3 to 26.7 milliequivalents per liter. The serum potassium was decreased from 5.2 to 4.4 milliequivalents per liter, the protein from 7.1 to 5.9 per cent, the cholesterol from 279 to 192 mg. per hundred cubic centimeters, the nonprotein nitrogen and sugar remained about the same and the hematocrit reading fell from 44.5 per cent to 37 per cent cells. Desoxycorticosterone was continued for six more days, from 10 to 15 mg. daily, and he gained another kilogram and had no rise in blood pressure. The urine volume remained about 10 per cent less than in the foreperiod, the nitrogen was 10 per cent less than in the foreperiod, the chloride was about 50 per cent of that of the foreperiod, the sodium about 50 per cent and the potassium excretion was increased about 25 per cent. The serum sodium continued elevated at 143.2, chloride at 108.8 milliequivalents per liter, bicarbonate at 27 milliequivalents per liter, nonprotein nitrogen fell from 32 to 21 mg. per hundred cubic centimeters and serum potassium, protein and sugar did not change during this additional six days on desoxycorticosterone. For the whole ten day period the extracellular fluid volume rose 2.3 liters and serum volume rose 800 cc. The hematocrit reading fell from 44.5 to 34 per cent cells. He was discharged to the clinic on 12.5 mg. of desoxycorticosterone given subcutaneously by himself daily with between 5 and 10 Gm. of sodium chloride added to the diet and has continued to gain weight. When last seen, two months after the start of desoxycorticosterone administration, he was feeling well, was gainfully employed and was maintaining a blood pressure of 120 systolic, 85 diastolic as well as a serum sodium of 140 and a potassium of 3.9 milliequivalents per liter. He never developed any peripheral edema but at times noted that his face was puffy.

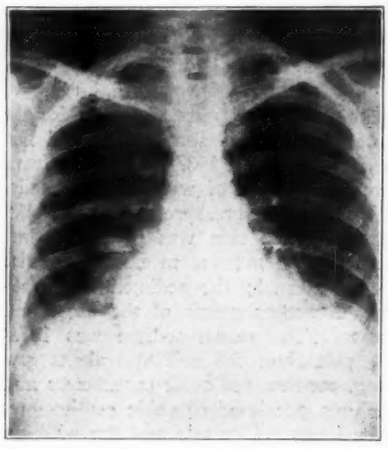

Fig. 5 (case 3).—Pulmonary congestion and dilatation of the right side of the heart associated with a gain of 11 Kg. during ten days' treatment with desoxycorticosterone propionate.

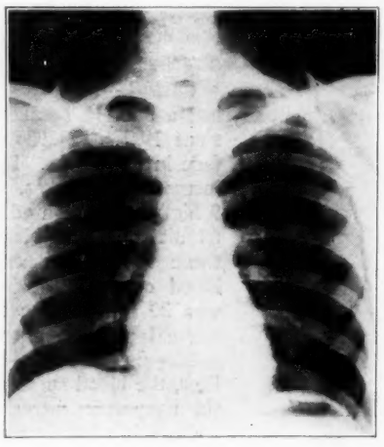

Fig. 6 (case 3).—Disappearance of pulmonary congestion and dilatation of the heart two weeks after the cessation of desoxycorticosterone propionate injections and the limitation of salt and water in the diet.

CASE 11.—*History.*—R. F., a man aged 33, married, an elevator operator, began to notice weakness, anorexia and loss of weight (60 pounds, 27 Kg., in all) in the fall of 1937. Over about the same period "brown spots" appeared on his skin. Following tonsillectomy on May 21, 1938, he began to have nausea and vomiting and was admitted to Bellevue Hospital, where he remained three and one-half months with the diagnosis of Addison's disease. The serum sodium at this time was 115.9 milliequivalents per liter. He responded well to sodium chloride but implantation of an adrenal gland into the right rectus was ineffective.

Sept. 12, 1938, he began visiting the Vanderbilt Clinic. He presented the classic picture of weakness, pigmentation of the skin and mucous membranes and a blood pressure of 95 systolic, 70 diastolic. He had a mild secondary anemia, x-ray examination of his chest showed healed tuberculosis at the left apex, and his adrenal areas contained shadows of calcium density. The serum sodium was 141 milliequivalents per liter, potassium 4.5 milliequivalents per liter, sugar 83 mg. per hundred cubic centimeters and nonprotein nitrogen 22 mg. per hundred cubic centimeters. On approximately 15 Gm. of sodium chloride and a low potassium diet he improved greatly.

Jan. 9, 1939, he was admitted to the Presbyterian Hospital acutely ill with hemolytic streptococcus sore throat. The serum sodium was 132 milliequivalents per liter. Again on February 20 he came into the hospital with fever. This lasted for more than a week and was never satisfactorily explained. Roentgenograms of the spine showed a destruction of the intervertebral disks between the fourth and fifth dorsal vertebrae suggesting tuberculosis, probably inactive. He was discharged March 11 with a relatively normal temperature, a blood pressure of 90/60, sedimentation rate 78 mm. in one hour and a calculated serum sodium of 137 milliequivalents per liter. He returned to the Vanderbilt Clinic for Doca administration April 3.

A man of 33, with classic Addison's disease due to tuberculosis, he survived two febrile episodes by the use of sodium chloride. He had inactive pulmonary and spinal tuberculosis.

Treatment with Desoxycorticosterone.—The patient was treated in the clinic. He was on his usual diet at home with from two to three teaspoonfuls of salt added to the diet. During the first week of the administration of desoxycorticosterone (15 mg. every two days) he gained 1.5 Kg. in weight and his blood pressure rose from 95/70 to 120/75. Serum chloride showed no change, his serum protein fell from 7.0 to 6.8 per cent, and his blood sugar remained constant at 65 to 75 mg. per hundred cubic centimeters. He was taught to inject the desoxycorticosterone himself at home and after seven weeks of 15 mg. every other day he gained 2.6 Kg. and maintained his blood pressure at the normal level of 120/80. His serum protein had fallen to 6.4 per cent, nonprotein nitrogen from 27 to 22 mg. per hundred cubic centimeters and serum chloride remained the same, about 106 milliequivalents per liter. He felt much improved, developed a large appetite, and although he stated that his ankles had been swollen at night, this edema had never been observed in the clinic in the morning. Three weeks after his last clinic visit and approximately two months after he had begun to take desoxycorticosterone he was admitted to the ward

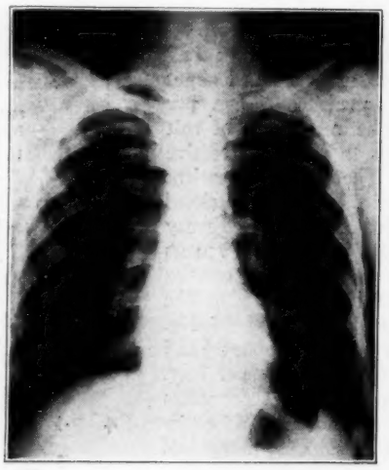

Fig. 7 (case 11).—Appearance of heart before treatment with desoxycorticosterone acetate.

Fig. 8 (case 11).—Appearance of heart after treatment with desoxycorticosterone acetate.

with a story of slowly increasing dyspnea for three weeks, severe enough in the past two weeks to confine him to his fifth floor room. This was accompanied by nonradiating squeezing, substernal pain. Two days before admission he had complained of nausea, vomiting and epigastric cramps. On examination he was dyspneic with slight cyanosis, and his face was puffy. Fine rales and dulness were present at the right base. The pulmonic second sound was greater than the aortic second sound. A tender liver was felt two fingerbreadths below the costal margin. There was no pitting edema. The temperature was 99.4, blood pressure 130/100, vital capacity 1,300 cc., venous pressure 140 mm. of water, rising to 200 following an infusion of 200 cc. of physiologic solution of sodium chloride. The circulation time was 64 seconds (calcium gluconate), serum sodium was 143.5 milliequivalents per liter, potassium 3.2 milliequivalents per liter, protein 6 per cent, sugar 80 mg. per hundred cubic centimeters. X-ray examination of the heart (fig. 8) showed marked increase in size both to the right and to the left, contrasting sharply with a normal cardiac contour shown on a roentgenogram taken four months earlier (fig. 7). An electrocardiogram showed little beyond the voltage lower than that of the record taken four months previously. The urine contained 3 plus albumin and no significant cells. Desoxycorticosterone and salt were withheld. On the day following admission, his blood pressure rose to 150/130 and because of increasing dyspnea and cyanosis together with a venous pressure of 250 mm. of water, he was digitalized parenterally, 400 cc. of blood was withdrawn by phlebotomy, and he was put in an oxygen tent. The following morning his temperature had risen to 103 F., venous pressure had fallen to 100 mm. of water and throughout the day his blood pressure fell from 130/80 to 60/40, responding only briefly to an infusion of 1,250 cc. of 5 per cent dextrose in saline solution. The heart sounds became poor, his pulse became irregular and he died the following morning after ten hours of coma with increasing tachypnea and irregular tachycardia. Postmortem examination revealed no gross cause for cardiac failure, although there was slight cardiac hypertrophy and marked dilatation. Only about 150 cc. of fluid was present in the pericardium, and a mild bronchopneumonia was also present. There was also advanced tuberculosis of both adrenal glands.

SUMMARY

1. The use of desoxycorticosterone esters in patients with Addison's disease produces striking clinical and physiologic effects.

2. Clinically there is unequivocal improvement far greater than has resulted from any therapy hitherto advocated.

3. The most striking physiologic effects are on salt and water metabolism. The administration of desoxycorticosterone esters causes retention of sodium and water. The result of this retention is an improvement in the patient's condition which is qualitatively identical with that following the administration of salt and water alone, but quantitatively it is far more marked.

4. No effect on carbohydrate metabolism has been observed.

5. Patients vary greatly in the amounts of desoxycorticosterone esters required to alleviate the manifestations of adrenal insufficiency.

6. Extreme caution must be exercised in the administration of desoxycorticosterone esters because excessive amounts may lead to the development of hypoproteinemia, marked edema and cardiac insufficiency.

ADDENDUM.—Since this article was written, it has been found that patients do most satisfactorily with small daily doses of synthetic hormone without the addition of salt beyond that of the usual diet. It may also be pointed out that patient 7 developed transient dilatation of the heart, relieved by the withdrawal of salt. Furthermore, patient 5 died suddenly at home while under treatment while the blood pressure was normal and without fever.

Clinical Notes, Suggestions and New Instruments

A DEVICE FOR TURNING THE FRAME PATIENT

HOMER STRYKER, M.D., ANN ARBOR, MICH.

Hospitals or physicians who use the anterior and posterior Bradford frames are confronted with the nursing problem of changing the patient from one frame to the other. A method which enables one nurse to turn any patient without lifting and with a minimum of discomfort to the patient is herein described. It has been found satisfactory in the daily care of from fifteen to twenty such patients at the University Hospital. If a patient who requires frame care is allowed to remain a part of the day on his abdomen, he is more comfortable and is less liable to develop decubital ulcers or respiratory or renal complications.

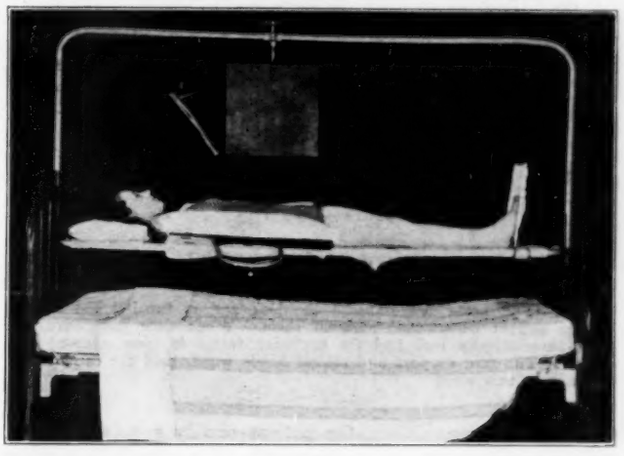

Fig. 1.—Patient on posterior Bradford frame with foot and arm supports attached. The frame is supported by the turning devices attached to the ends of the bed. These also support the overhead frame, from which is suspended a small cabinet the door of which serves as a reading board or, when lowered, a writing board.

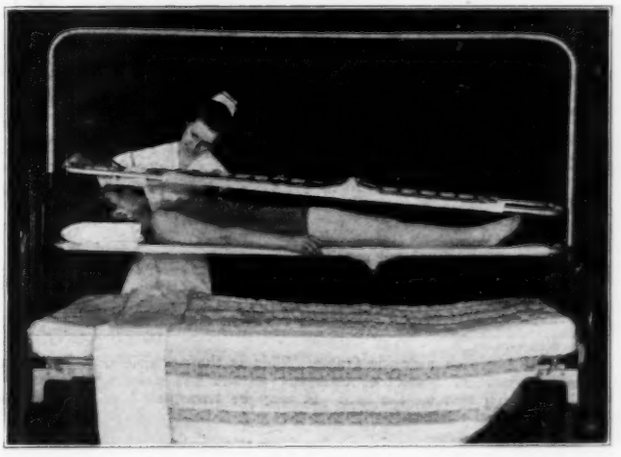

Fig. 2.—The nurse has removed the cabinet and the arm and foot supports and is placing the anterior frame down over the patient, where it is fastened by a wing nut at each end.

METHOD OF TURNING PATIENT

The patient is placed on his back on a posterior frame. This frame is then suspended about 1 foot from the mattress, each end being attached to a turning device which clamps on to the

From the Orthopedic Service of Dr. Carl E. Badgley.
From the Department of Surgery, University of Michigan Medical School.

head and foot of the bed. To turn the patient, the anterior frame is placed over him and pressed down firmly, pressing him between the two frames. The anterior frame is then locked in this position. The nurse then releases a spring lock at the end and revolves the two frames, with the patient between them, through an angle of 180 degrees, whereupon the frames automatically lock again, leaving the patient face downward on

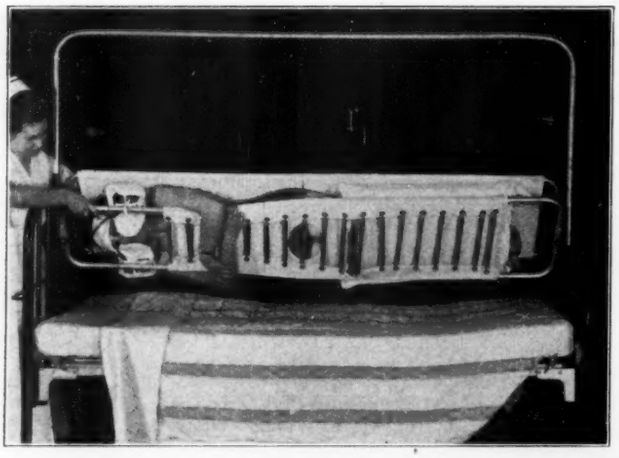

Fig. 3.—The nurse has released the lock and is turning the frames with the patient compressed between them. When face downward the frames automatically lock and the posterior frame is then released and lifted off. The face support and rubber bands which hold the canvas taut are shown in this view.

the anterior frame. Since the patient simply revolves on his long axis without change of the center of gravity, little effort is required for the turning. The upper frame (posterior) is now released and lifted off.

While on the anterior frame, the head is supported by an adjustable face piece which lies on the anterior frame and takes the weight on the cheeks and forehead. It is padded with sponge rubber and has flannel covers which may be removed

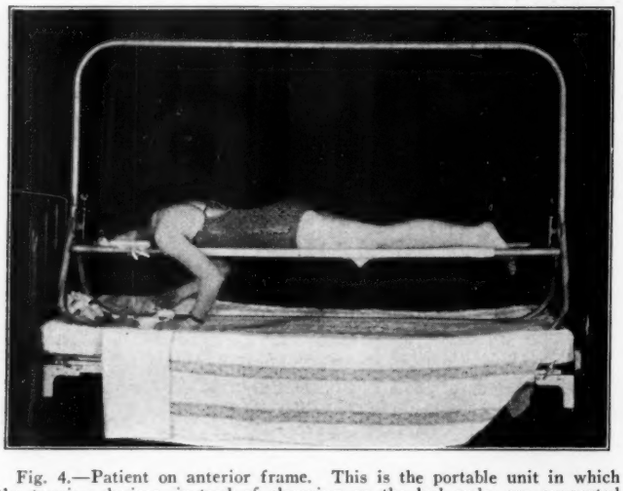

Fig. 4.—Patient on anterior frame. This is the portable unit in which the turning devices, instead of clamping on the bed ends, are supported by a base which sets on the bed. It may be transported as a unit and rests on any level surface.

for washing. The eyes are about 15 inches from the mattress, a comfortable distance for reading and writing. The anterior frame is narrowed at the shoulders to allow the arms to be brought down over the sides for comfort. In some cases frequent turning may be required, but usually the patient remains on the anterior frame during the day. At night the patient is turned in the same manner to the posterior frame.

TYPE OF FRAMES

By means of turn buckles at each end, the adult frames are adjustable in width between 12 and 17 inches, children's from 7 to 12 inches. No patient requires a frame more than 17 inches in width—over this it becomes a hammock and no longer effectively supports the spine.

Our frames are made of light weight tubing but gas pipe frames of proper length may be used with the turners by drilling a five-eighths inch hole in the center of each end by which they are fastened to the turning disk. For a standard bed they should be 6 feet 3 inches long and for the portable unit they are 6 feet 1 inch long.

COVERING OF FRAMES

The frames are covered with heavy canvas, with eyelets at 4 inch intervals along each side, and wide enough to fold over the sides of the frame when set at its greatest width. Bands of rubber stretched across the back between the eyelets are used in place of laces or straps with buckles. This keeps the canvas perpetually and evenly taut, provides for personal variations in contour and allows changing the width of the frame without removal of the frame covers. They are easily applied or removed and eliminate the necessity of frequent adjustment. A spreader is placed beneath the center of each frame to maintain uniform width. The canvas is padded with celotex or 1 inch sponge rubber, over which a draw sheet is placed and pinned beneath the frame. A 6 inch opening at the center allows toilet service. The small (6 inch diameter) chamber

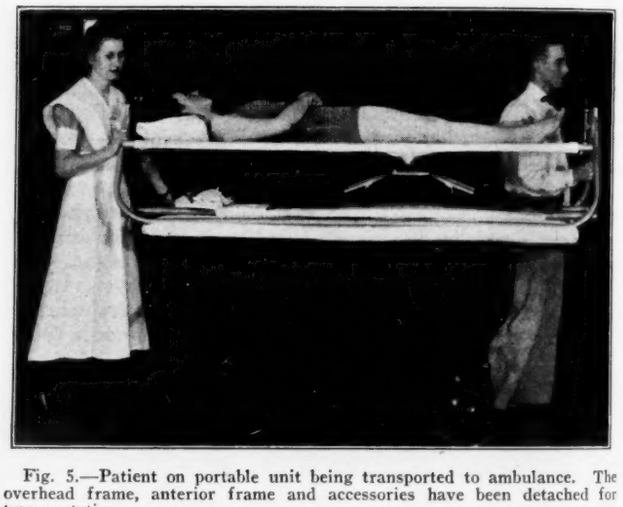

Fig. 5.—Patient on portable unit being transported to ambulance. The overhead frame, anterior frame and accessories have been detached for transportation.

mug commonly used for infants will be found more satisfactory than the conventional bedpan. It can be lifted up through the opening overlapping the edge of the canvas, which prevents soiling.

SUPPORTS FOR ARMS AND FEET

Attachments are provided for the support of the feet at right angles and for the arms at the sides of the frame. These are easily applied or removed while the patient is on the frame. The arm supports may also be used to hold the tray at mealtime.

TYPE OF BED

The turners fit on the head and foot of any standard hospital bed of either round or square design. A socket is provided on top of each turning device for the insertion of an overhead frame if desired. The turners may be used for this purpose with or without the Bradford frames. A cabinet with a reading board may be suspended from the overhead frame.

PORTABLE UNIT

For those patients who require a continuation of frame care at home or elsewhere, a portable unit is provided in which the turning device is fastened to a base which sets on the bed at the hospital or at home and may be transferred with the patient as a unit in an ambulance or invalid car. This has been especially appreciated when there is only one person available in the home to care for the patient.

1101 Baldwin Avenue.

THREE FATAL CASES OF SODIUM NITRITE POISONING

LOUIS R. PADBERG, M.D., AND THOMAS MARTIN, M.D.
Coroner and Autopsy Physician, Respectively
ST. LOUIS

Sodium nitrite and other inorganic nitrites are used mainly in the manufacture of dyestuffs and more recently as anti-corrosives in automobile anti-freeze mixtures. Inorganic nitrites are rarely encountered as the cause of human poisoning. It is therefore considered of value to report the following cases:

Three white men, J. N., aged 55, T. H., aged 65, and A. K., aged 70, were inmates of a cheap lodging house near the river front, the location of several wholesale chemical companies, one of which is a large distributor of sodium nitrite. Oct. 27, 1938, at about noon these three men were observed preparing a meal consisting of "beef stew" in the room of J. N. Four hours later the landlady of the house saw A. K. staggering down the stairs; when he reached the bottom he collapsed without making a statement. The landlady stated that the man's face was very pale and that his lips and the areas around the lips were purplish. The City Hospital ambulance was called, and all three men were pronounced dead on arrival at the hospital.

The bodies were immediately taken to the city morgue, where autopsies were performed.

SUMMARY OF AUTOPSIES

Gross examination of the three bodies showed the following conditions in each body:

The skin was very cyanotic, about the color of slate; the blood was thin and did not coagulate and was a dark brown, simulating prune juice.

Specifically the results of the examination in each are recorded as follows:

J. N. was 5 feet 8 inches (173 cm.) tall and weighed 140 pounds (63.5 Kg.). The hair was white and the eyes were blue; the left forearm had been amputated below the elbow. Dense fibrotic adhesions were seen in the right pleural cavity and old fibrosis was present throughout the right lung, particularly in the apex. The capsule of the kidney was adherent and did not strip readily. Other than this there were no gross abnormalities.

T. H. was 5 feet 11 inches (180 cm.) tall and weighed 175 pounds (79.4 Kg.). The hair was white and the eyes were blue. There was edema of the brain and lungs, hypertrophy of the heart, moderate sclerosis of the vessels and degenerative changes within the kidney.

A. K. was 5 feet 10 inches (178 cm.) tall and weighed 180 pounds (81.6 Kg.). The hair was white and the eyes were blue. There was edema of the brain and lungs, hypertrophy of the heart with atheromatous changes in the aorta and sclerosis of the coronary. The arteries were moderately sclerosed and the kidney showed some parenchymatous changes. Other than these abnormalities the gross examination of all viscera except the stomach was negative.

The three deaths occurring almost simultaneously after a meal might have been suggestive of botulism except that the time factor was too short and the food eaten was known to have been cooked. The viscera and blood samples of the three men together with a portion of the "stew," a box of salt and pepper and an ice cream carton containing a yellowish white crystalline substance were submitted to the coroner's toxicologist for chemical examination. Within forty-eight hours the following report was received:

On acid steam distillation of 100 Gm. portions of each portion of stomach and contents there was chemically detected in the dilute sodium hydroxide of the receiver the presence of a nitrite. A portion of this nitrite was subsequently isolated as silver nitrite and so identified. A quantitative analysis was performed on steam distillates from weighed portions of stomach and contents by the method of Lunge. Approximate amounts of nitrite, calculated as sodium nitrite and based on total weights of stomach and contents, are as follows: in J. N., 0.5 Gm. of sodium nitrite; in T. H., 0.7 Gm., and in A. K., 0.1 Gm.

Samples of the blood of the three men were submitted to spectroscopic examination for the presence of methemoglobin: A strong absorption band of methemoglobin (630) was observed at 1:100 dilution, p_H 7.1, in all three samples.

A portion of food containing meat and tomatoes was submitted to acid steam distillation and the presence of a nitrite was detected in the distillate.

The sample of salt and pepper was examined and found to be sodium chloride and finely ground black pepper.

Seventy-five Gm. of a yellowish white crystalline substance contained in an ice cream carton was submitted to analysis and found to be almost chemically pure sodium nitrite.

A thorough investigation was made as to the motive, but up to the present time these cases are unsolved, i. e. as to whether they were accidental, suicidal or homicidal.

1300 Clark Avenue.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, SECRETARY.

POLYTHERM SHORT WAVE APPARATUS ACCEPTABLE

Manufacturer: Polytherm, Incorporated, 707 Broadway, Paterson, N. J.

The Polytherm Short Wave Apparatus considered in this report includes the "Advance," "Standard Cabinet" and "Portable" models. These units are identical in circuit and component parts. They are designed for use in medical and minor surgical diathermy. Standard equipment includes pad electrodes, felt spacers and surgical accessories.

Polytherm Short Wave Apparatus.

Two tubes (211-B) are employed in a typical tuned-plate, tuned-grid circuit, operating at approximately 14 meters wavelength. There is a ventilator to dissipate heat from the tubes by convection. The bipolar surgery which is optional on any unit is the introduction of one terminal which is a tap on the output or pick-up coil.

The Council tests showed that with an input of 610 watts and an electromotive force of 120 volts, the maximum output obtainable was 245 watts. After two hours of operation at a maximum input of 610 watts the Council tests demonstrated a final temperature in the outside windings of the transformer which stayed within allowable limits.

The firm submitted evidence to substantiate the efficacy of the machine in producing a temperature rise in the human thigh

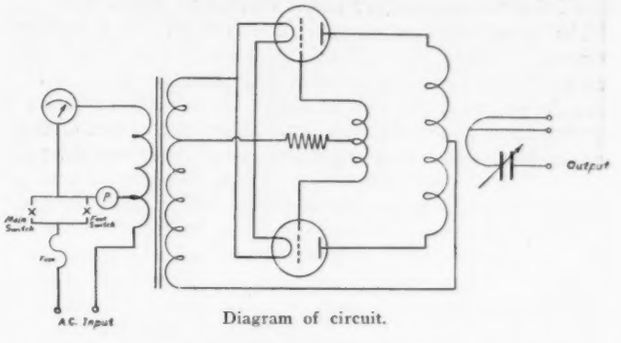

Diagram of circuit.

with the cuff technic. A reliable investigator was secured by the firm to perform these tests. Six tests were carried out and three normal male subjects were used. Cuffs measuring 17¾ by 4¾ inches were wrapped about the thigh, 7½ inches apart. The average spacing was 1⅛ inches for the right and 1¼ inches for the left. Temperature measurements were taken by thermocouples before and after twenty minute treatments. The thermocouples were inserted into the subcutaneous and intramuscular

tissue in the usual manner. Rectal temperatures were observed. The average room temperature was 76 F. The room humidity was 72 per cent.

Average temperatures (F.) of six observations after applying heat for twenty minutes are given in the accompanying table.

Average Temperatures of Six Observations

Deep Muscle		Rectal	
Initial	Final	Initial	Final
97.9	107.2	99.5	99.6

The unit was investigated clinically by the Council and found to give satisfactory service.

In view of the foregoing report, the Council on Physical Therapy voted to accept the Polytherm Short Wave Apparatus, "Advance," "Standard Cabinet" and "Portable" Models, for inclusion in its list of accepted devices for use with the cuff technic.

TROPIDORES ACCEPTABLE

Manufacturer: Hill Laboratories Company, 128 Lancaster Avenue, Wayne, Pa.

The Tropidores is a device for continuous, local, heated air therapy. The system consists of the moving of warm air through flexible garments that may be applied locally and worn for as long as desired on the affected parts of the body. The unit is portable, the machine being small enough to be put on an ordinary bedside table. The complete assembly consists of (1) the motor, intake fan and heating coil chamber, (2) master conveying tube and connecting tubes, (3) two boots for the legs (hip length), (4) one sleeve and (5) jacket for the treatment of thorax and torso regions, supplied separately and made up according to specifications.

Tropidores.

The manufacturer states that the Tropidores is designed to induce heat controllable at any desired degree up to 145 F., which temperature is claimed to be safe when constantly applied on the full length of the extremities without danger of shock or evidence of rise of temperature in the mouth. Heated air by means of a fan with a capacity of 30 cubic feet per minute is blown through a tube. The total consumption of electricity when a standard coil is used is 230 watts an hour. The apparatus may be attached to an ordinary electric light socket by a 12 foot cable and will be supplied for alternating or direct current as specified.

The large hose from the machine is fitted into a three way connection leading to smaller hose and to the vestibules, which are at one end of each garment and allow the passage of air into the garments through numerous holes. All vestibules are removable to permit sterilization. The garments are of canvas and supplied with flannel trimmings at all body contact points, slide fasteners and draw strings. They are supposed to provide freedom of arm and leg movement and to allow the patient to turn in bed without readjusting the apparatus. The hose are also flexible. Heavy woolen stockings and gloves should be worn under Tropidores garments for the purpose of absorbing perspiration, which acts as a humidifier of inducted air. Slide fasteners should be left partly open to permit a constant flow of air.

An investigation of the unit was conducted by the Council, from which study it appeared probable that the Tropidores offers a convenient form of heated air therapy for those who are bedfast. It is necessary that an attendant, trained in the use of this apparatus, supervise the treatments, because it is possible to create unduly heated areas close to the entrance of the heated air into the garment. If the treatments are of long duration, caution must be exercised lest the sweating be so prolonged as to cause weakness. Some restlessness and fatigue also were shown by those who were treated over four hours. It was found further, as might be expected, that there was a drop of temperature of about 15 or 20 F. from the original before the air reached the joints of the extremities.

In the light of the foregoing report, the Council on Physical Therapy voted to include the Tropidores in its list of accepted devices.

Council on Pharmacy and Chemistry

REPORTS OF THE COUNCIL

THE COUNCIL HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

PAUL NICHOLAS LEECH, Secretary.

DILANTIN SODIUM

Sodium 5, 5-diphenyl hydantoinate, originally presented to the Council under the name "Dilantin" and marketed as "Kapseals Dilantin" by Parke, Davis & Company, has been redesignated "Dilantin Sodium" and is now marketed as "Kapseals Dilantin Sodium." Dilantin Sodium is an active anticonvulsant and relatively feeble hypnotic, used in the treatment of epilepsy. H. H. Merritt and Trace J. Putnam studied the anticonvulsant action of a number of drugs, including Dilantin Sodium,[1] and later they reported[2] the results of the treatment of 150 epileptic patients with this drug. The Council also received a report of the treatment of fifty-two epileptic children by Dr. O. P. Kimball of Cleveland. While these clinical studies pointed to the therapeutic value of Dilantin Sodium the Council requested additional information, with especial reference to the toxicology, the side actions and the limitations of its usefulness.

The Comparative Effectiveness of Various Anticonvulsant Drugs in 595 Epileptic Patients

	Drug or Drugs Most Effective								
Investigator	A	B	C	D	E	A and B Equally Effective	Neither A nor B Effective	No Analyzable Comment	Total No. of Patients
Weaver et al.	6	..	2	..	..	..	..	6	14
Wexberg	2	2	..	..	..	2	..	1	7
Spurling et al.	7	..	3	1†	..	1	..	3	15
Bigler	9	1	1	2	..	4	1	1	19
Reese	42	4	2	3	1	4	2	3	61
Fetterman	10	1	..	..	..	..	1	8	20
Taylor	14	..	..	..	..	..	6	..	20
McNeil	4	12	..	..	..	..	..	..	16
Kimball	100	..	..	..	..	..	29	..	129
Dixon	22*	..	..	..	..	2	2	15	41
Osgood	24	4	..	..	..	13	2	..	43
Philips	8	..	..	..	..	..	..	..	8
Merritt	156	3	..	..	..	..	27	16	202
Totals	404	27	8	6	1	26	70	53	595

A, Dilantin Sodium; B, phenobarbital; C, dilantin plus phenobarbital; D, phenobarbital plus bromides; E, bromides.

* The Council's referee accepted this figure without verifying it.

† Dilantin plus bromides.

Pharmacologic studies were conducted in the laboratories of Parke, Davis and Company, and clinical investigations were made in a number of institutions, five of them in institutions for the treatment of epilepsy and kindred conditions.

The pharmacologic studies show that Dilantin Sodium is of relatively low toxicity when administered orally to rats, rabbits and dogs, and much more toxic when injected intravenously. A special investigation was conducted to show whether Dilantin Sodium interferes with the utilization of ascorbic acid, after Kimball had reported hyperplasia of the gums suggestive of

1. Merritt, H. H., and Putnam, T. J.: A New Series of Anticonvulsant Drugs Tested by Experiments on Animals, Arch. Neurol. & Psychiat. **39:** 1003 (May) 1938.

2. Merritt, H. H., and Putnam, T. J.: Sodium Diphenyl Hydantoinate in the Treatment of Convulsive Disorders, J. A. M. A. **111:** 1068 (Sept. 17) 1938.

scurvy. The results of the experiments on animals did not indicate that the drug has any influence on the utilization of ascorbic acid.

Physicians who studied Dilantin Sodium therapeutically were furnished with forms for recording data. Some sixty pages of these forms were submitted to the Council by the firm, which received them from ten observers who had treated 437 patients. The headings of the forms included history, age, sex, age at onset, etiology, type of attacks, reactions and treatment, including dosages and a comparison of results with phenobarbital and Dilantin Sodium.

The side actions reported by one or more include dizziness, dry skin, dermatitis, rash, itching, tremors, fever with temperature of 104 F. in one case, nausea, vomiting, blurred vision, fatigue, apathy, difficult breathing and swallowing, nervousness, mental confusion and active hallucinations. Hyperplasia of the gums has been reported by Kimball.

It would require much space to present a summary of the work of every one of the clinical investigators, but it is believed that the accompanying table submitted by Parke, Davis and Company (and confirmed by the Council's referee) affords a fair statement of the chief points of interest.

The Council voted that the firm be informed (1) that the available evidence justifies the recognition of Dilantin Sodium as a therapeutic agent of promising value in the treatment of many cases of epilepsy and (2) that Dilantin Sodium will be accepted for inclusion in N. N. R. provided the firm will agree to market it under rigid restrictions, including those which further experience shall indicate, as well as the following: (*a*) It shall not be recommended for use by the general practitioner unless he is able to maintain a close (daily) supervision of the patient, until the scope of its usefulness as well as its side actions have been determined more accurately; (*b*) it is not to be recommended for the treatment of those patients whose seizures occur only at long intervals unless moderate doses of phenobarbital are ineffective or induce disagreeable side actions. The firm has agreed to these conditions. The A. M. A. Chemical Laboratory has found the composition of Dilantin Sodium satisfactory.

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

DILANTIN SODIUM.—Sodium 5,5-diphenyl-hydantoinate. —Sodium 2,4-diketo-5,5-diphenyl-tetrahydroglyoxaline. — The mono-sodium salt of 5,5-diphenyl-hydantoin,

$$Na(C_6H_5)_2C.NH.CO:N.C:O.$$

Actions and Uses.—Dilantin sodium is an anticonvulsant with a relatively weak hypnotic action. It is used in the treatment of epileptic patients who are not benefited by phenobarbital or bromides and those in whom these drugs induce disagreeable side actions. Dilantin sodium appears to be more effective in controlling seizures of the grand mal type than in those of the petit mal. It does not cure congenital mental defects or the mental deterioration often observed in the epileptic. Various side actions of different degrees of severity which have been observed include dizziness, dry skin, dermatitis, rash, itching, tremors, fever, nausea, vomiting, blurred vision, fatigue, apathy, difficult breathing and swallowing, nervousness, mental confusion and active hallucinations, and hyperplasia of the gums suggestive of scurvy, though its use does not interfere with the utilization of vitamin C. Dilantin sodium is strongly alkaline and it may give rise to gastric irritation.

Dosage.—The optimum dosage of dilantin sodium must be determined by the daily observation of its effects by the physician. The influence of the drug on seizures and the appearance of any of the side actions enumerated must be a guide to the dosage. Mild symptoms do not necessarily require that the dosage be stopped. The beginning adult dose is 0.1 Gm. (1½ grains) with at least half a glass of water three times daily. If necessary this dose may be increased gradually to 0.2 Gm. (3 grains) three times daily. Children above the age of 6 years may be given 0.1 Gm. (1½ grains) three times daily for one week, after which it may be increased if necessary to 0.1 Gm. (1½ grains) four times daily with at least half a glass of water to prevent gastric irritation due to the alkalinity. Dilantin sodium is more rapidly effective if given before meals, but should it cause gastric irritation it should be given immediately after meals. Children under 4 years of age may start with 0.03 Gm. (one-half grain) mixed with cream (to disguise the bitter taste and to prevent gastric irritation) twice a day. Obviously such doses require the most careful supervision. If this dose is borne without side actions the dosage may be increased to 0.03 Gm. (one-half grain) three or four times a day. Every slight increase in dosage is made only after the physician is convinced that such increase is necessary and that no harm is to be anticipated.

The transition from phenobarbital, bromides or other hypnotic-type drugs to dilantin sodium should be made gradually with some overlapping in dosage. By this procedure the danger of phenobarbital or bromide withdrawal symptoms (increased number of seizures) is minimized, and side actions incident to the beginning administration of Dilantin Sodium are lessened.

Manufactured by Parke, Davis & Co., Detroit. No U. S patent. U. S. trademark applied for.

Kapseals Dilantin Sodium 0.1 Gm. (1½ grains): Each kapseal (hermetically sealed capsule) contains 0.1 Gm. (1½ grains) of sodium 5,5-diphenyl hydantoinate.

Kapseals Dilantin Sodium 0.03 Gm. (½ grain): Each kapseal (hermetically sealed capsule) contains 0.03 Gm. (½ grain) of sodium 5,5-diphenyl hydantoinate.

Dilantin sodium occurs as an odorless, white, microcrystalline powder, possessing a slightly bitter taste. It is soluble in alcohol and glacial acetic acid; practically insoluble in ether, petroleum ether and benzene. Aqueous solutions of dilantin sodium yield an opalescent crystalline precipitate of diphenyl-hydantoin, which dissolves when the *pH* of the mixture is adjusted to 11.7.

Dissolve about 0.25 Gm. of dilantin sodium in 5 cc. of boiled water: the mixture should not require more than 1 cc. of tenth-normal alkali to produce a clear, colorless solution; add an excess of diluted hydrochloric acid, shake thoroughly, collect the precipitated diphenyl-hydantoin on a filter paper, wash with water and dry at 95 C.: it melts at 293-299 C. with decomposition.

Treat about 0.5 Gm. of dilantin sodium with 10 cc. of solution of sodium hypochlorite, heat to 50 C., pass in carbon dioxide; collect the precipitate formed on a filter paper. Dry the precipitate in a partial vacuum and recrystallize from chloroform: the melting point of the 5,5-diphenyl-1,3-dichloro-hydantoin lies between 163 and 167 C.

Incinerate about 0.2 Gm. of dilantin sodium: the residue responds to tests for sodium carbonate.

Dissolve about 0.5 Gm. of dilantin sodium in 100 cc. of water, add 5 cc. of diluted nitric acid, shake and filter through paper: separate portions of 10 cc. each of the filtrate yield no greater opalescence on addition of 1 cc. of silver nitrate solution than that produced by 0.25 cc. of tenth normal hydrochloric acid in 50 cc. of water (*chlorides*) or no appreciable turbidity on the addition of 1 cc. of barium nitrate solution (*sulfates*). Acidify about 0.2 Gm. of dilantin sodium in 50 cc. of water with diluted hydrochloric acid, using litmus paper as the indicator; filter through paper: a 10 cc. portion of the filtrate yields no color or precipitate on saturating with hydrogen sulfide (*salts of heavy metals*). Dissolve 0.1 Gm. of dilantin sodium in 5 cc. of sulfuric acid: the color produced should not be greater than that yielded by 0.1 mg. of benzilic acid in 5 cc. of sulfuric acid.

Heat about 0.5 Gm. of dilantin sodium, accurately weighed, to constant weight at 95 C.: the loss in weight should not exceed 2.5 per cent. Transfer about 0.25 Gm. of the dry dilantin sodium, accurately weighed, to a separatory funnel, add 50 cc. of water and 10 cc. of diluted hydrochloric acid; extract the mixture with 100 cc. of ether and repeat the extraction with four successive 25 cc. portions of ether; evaporate the combined ether extracts in a tared beaker and dry to constant weight at 95 C.: the 5,5-diphenyl-hydantoin should amount to not less than 90.6 per cent, nor more than 92.0 per cent of the dry sample, and should melt above 292 C.

FUNGUS EXTRACTS-ABBOTT.—Liquids obtained by extracting dried spores with a menstruum consisting of equal volumes of glycerin and a solution containing sodium chloride 5 Gm. and sodium bicarbonate 2.7 Gm. in distilled water 1,000 cc.

Actions and Uses.—See general article Allergenic Protein Preparations, New and Nonofficial Remedies, 1939, p. 27.

Dosage.—See general article Allergenic Protein Preparations, New and Nonofficial Remedies, 1939, p. 27.

Fungus Extracts-Abbott are marketed in 2 cc., 5 cc. and 30 cc. vials.

Manufactured by the Abbott Laboratories, North Chicago, Ill. No U. S. patent or trademark.

Alternaria spp. Fungus Extract-Abbott; Aspergillus fumigatus Fungus Extract-Abbott; Aspergillus niger Group Fungus Extract-Abbott; Cephalothecium roseum Fungus Extract-Abbott; Hormodendrum spp. Fungus Extract-Abbott; Monilia sitophilia Fungus Extract-Abbott; Mucor spp. Fungus Extract-Abbott; Penicillium rubrum Fungus Extract-Abbott; Ustillago zeae (Corn Smut) Fungus Extract-Abbott; Yeast Fungus Extract-Abbott.

The yeast extract is prepared from dried brewers' yeast; the *Alternaria spp.* extract is prepared from the dried mass of spores with its supporting mycelium; the other extracts are prepared from the dried spores alone. The material is extracted at room temperature with a menstruum consisting of equal volumes of glycerin and a solution containing sodium chloride 5 Gm. and sodium bicarbonate 2.7 Gm. in distilled water 1,000 cc. for from four to five days and is clarified and sterilized by Berkefeld filtration. The finished liquid is a 5% W/V extract of the dried fungus material, each cubic centimeter representing 0.05 Gm. of dried material.

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SATURDAY, NOVEMBER 4, 1939

MEDICAL SERVICE IN A TEACHING HOSPITAL—DR. CHRISTIAN'S "FAREWELL REPORT"

Medicine has developed through the labor of many and under the leadership of relatively few. During the past half century medicine in general, and American medicine in particular, have undergone revolutionary changes. The mystic, religious and philosophical domination has given way to the influence of natural and social sciences. The beneficial yield of objectivity to human society has surpassed the most optimistic expectations. Will the importance of personal leadership wane in the light of these recent changes? A superficial analysis of this problem might suggest that the introduction of exact sciences into medicine has decreased considerably the need for leadership. A more detailed study of the question indicates however that, precisely because of the rapid growth and of the diversified interests represented in modern medicine, guidance and correlation in medical education and practice are becoming more important than ever.

The Peter Bent Brigham Hospital under the leadership of Dr. Henry A. Christian and the late Dr. Harvey Cushing assumed a significant role in the establishment of modern clinical medicine in America. When the doors of this university clinic opened in 1913, it was one of the few institutions in the country which especially cultivated scientific clinical medicine. Since then fortunately the situation has changed. Now there are a number of important medical centers which represent different experiments in medical education. For this reason Dr. Christian's "farewell report" in the twenty-fifth Annual Report of the Peter Bent Brigham Hospital is of particular interest.[1] Here is the advice of a physician in chief who during a quarter of a century observed intimately the development of American medicine.

Dr. Christian describes what he believes should be the aims and the spirit of a medical service in a hospital. He points out that he who directs a hospital service must have a plan, a method, an ideal of perfection. The service must represent the highest accomplishment of leadership. Time and conditions change rapidly. Hence always there must be a willingness to meet changing conditions. A spirit of friendly helpfulness should pervade both the practical care of the patient and the scientific study of the medical problem. The best possible professional care should be administered to the patient in such a way that he feels that all in the hospital are interested in him as an individual. To the students and to the young physicians should be given a training with a broad foundation on which they can build themselves into the best type of clinicians. In such a training the art of good observation, the cultivation of memory, of logic and of technical skill, as well as the development of personality are essential. Diagnostic opinions should be expressed clearly and in writing. Dr. Christian states that ". . . often cowardice prevents such commitments." He criticizes the present tendency to say that the mass of literature is so great that no one can keep up with it. "To my mind this is but an excuse of the lazy." Specialization is essential but must be based on broad experience. He quotes Osler, who spoke of Jonathan Hutchinson as ". . . the only great generalized specialist which the profession has produced."

Dr. Christian, referring to himself, says ". . . the hospital physician busied daily in the care of patients, in contact with students, resident staff, associates and colleagues; this seemed to me the acme of attainment when in the days of my youth I dreamed dreams."

Traditions are to be cherished only if they represent the best in the professions. It is for this reason that Dr. Christian's report, an expression of need for a harmonious balance in medicine, is of importance to the profession.

1. Report of the Physician-in-Chief, Twenty-Fifth Annual Report of the Peter Bent Brigham Hospital for the year 1938, 1939, p. 92.

A NEW INTERPRETATION OF A PARAGRAPH IN THE HIPPOCRATIC OATH

The paragraph referring to lithotomy in the Hippocratic Oath, *οὐ τεμέω δὲ οὐδὲ μὴν λιθιῶντας, ἐκχωρήσω δὲ ἐργάτῃσιν ἀνδράσι πρήξιος τῆσδε,* is one of the most confusing in classical literature. It has been generally assumed that the oath forbids the performance of lithotomy. The two usual justifications for this injunction are (1) that the operation was often fatal and was therefore delegated to another expert group, and (2) that the oath indicates the beginning of specialization in Greek medicine as already existed in Egypt. These appear to a recent student of history to be absurd. Savas Nittis[1] states that sufficient grammatical and linguistic consideration has never been given to this paragraph. Instead a meaning was assumed and explanations for the injunction against lithotomy were sought afterward. Nittis proposes a new interpretation of the paragraph. His translation, for which gram-

1. Nittis, Savas: The Hippocratic Oath in Reference to Lithotomy: A New Interpretation with Historical Notes on Castration, Bull. Hist. Med. **7**: 719 (July) 1939.

matical and etymological reasons are given, would be as follows: "I will not cut, indeed not even sufferers from stone, and I will keep apart from men engaging in this deed." Since surgery could not be forbidden in those early times, the injunction in the oath, it is said, must refer to some abomination, such as castration, since *τέμνειν* means "to castrate."

Lithiasis was a common complaint in the early centuries in the Near East and still is. It must have required much attention by physicians; then instruments were invented for locating stone in the bladder. Who would seriously contend, therefore, that the ethical surgeon who performed these diagnostic procedures was prevented from doing lithotomy by an oral oath or a written contract? Celsus, who described lithotomy in the first century, was copying from an earlier Greek source. Comment by Aretaeos indicates that lithotomy was frequently performed by the best representatives of the Hippocratic school. Naturally serious complications often followed such an operation. Death frequently ensued and, if the patient survived, a resulting fistula often made life unbearable. Since the only relief came from cutting in the region of the urethral orifice of the bladder, necrosis of the testicles must have frequently followed lithotomies as a result of occlusion of the spermatic artery. Since it would have been easier for the surgeon to remove the interfering external genitalia before the lithotomy was performed, Nittis suggests, that practice was probably followed by some surgeons. Indeed, Nittis asserts that castration probably was the most frequently performed operation in ancient times.

In the Odyssey there is mention of an establishment where men were sent for castration. Herodotus speaks of one Panionios, of Chios, who "made his living from a most unholy trade. Whenever he came into possession of boys with good looks he castrated them and, bringing them to Sardis and Ephesus, sold them for a good price." In Rome, where the vices of Greece were imitated, castration for commercial or immoral purposes was usually carried out by the magnones, a special group of practitioners. While the regular physician probably performed castrations occasionally for some legitimate cause, neither Hippocrates nor Aristotle advised castration. During the early Christian era the number of castrates must have been impressive, for the first Ecumenical Council of Nice provided in its first canon to permit holy orders to a man "if he had been castrated by a physician on account of illness." During the Middle Ages, castration was advocated for the cure or prevention of many diseases, and until recently it was sometimes performed for the cure of epilepsy. In Europe following the renaissance, castration found widespread application for the prevention and cure of hernia. The general opinion that the castrated singers in the churches of Rome did not suffer from hernia promoted the idea. During the eighteenth century this abuse reached alarming proportions. The physician was free to use or abuse his judgment without legal restrictions in Greek society. Laws did not exist to penalize the physician or to award damages for malpractice to the patient or his family. In the oath, Hippocrates attempted to formulate the essential moral obligations of the physician and, according to Nittis, to prevent the practice of this abominable operation.

TRAVELING FACULTIES IN GRADUATE MEDICAL EDUCATION

The problem of continuation study for practicing physicians is no longer one concerned exclusively with education; transportation is beginning to be of considerable importance. A graduate program may be quite sound educationally and yet fail if it does not bring competent instructors to physicians desirous of continuing their studies. This is especially true in the more sparsely settled areas of the United States and in those states without medical schools.

For the past five years the physicians of Idaho have appreciated the need for continuation study. To meet this need they have brought to the five day annual meeting of their state association a flying medical faculty. Each year five or six instructors from one medical school have been invited to organize an integrated, correlated course of study of general interest to practicing physicians. Instruction in basic sciences has initiated discussions of clinical studies, and round table discussions have permitted attending physicians to participate. Expenses of the traveling faculty have been paid by the state association, since registration fees of $5 or $10 have been adequate to finance these programs.

In 1939 the state medical associations of Washington and Oregon arranged their annual meetings to utilize the same traveling faculty as was engaged in Idaho. Thus the physicians of three states have had the opportunity to attend, at their annual meetings, a continuation course. Attendance has been enhanced, and it has been possible to bring to each state systematic instruction at less expense than is ordinarily required.

Four other western states, Colorado, Utah, New Mexico and Wyoming, have pooled their interests in graduate studies to bring, every two years to one of their states, twenty out of state speakers to discuss problems of medicine and public health which are peculiar to the Rocky Mountain region. The medical society in each state has been represented on the executive committee and a different state society has acted as host every two years. The first Rocky Mountain Conference was held in Denver in 1937, the second in Salt Lake City in 1939, and the next meeting is scheduled for Wyoming. A registration fee of $3 has been sufficient to finance this effort.

Thus seven states, five without a four year medical school within the borders of the state, have provided

See Graduate Medical Education: Idaho, Oregon and Washington, in the Organization Section, this issue.

graduate opportunities for practicing physicians. Frequently physicians travel from 100 to 250 miles to attend one or two day regional meetings.

There still remain, however, physicians who are unable to leave their practice even for a short time to travel the distance required. For them provision is now being made, the instructors traveling throughout the state so that continuation study may be brought to a greater number of communities.

Current Comment

NOBEL PRIZE TO PROFESSOR DOMAGK

The Nobel Prize for Medicine was recently awarded to Prof. Gerhard Domagk, whose name is indelibly associated with the drug sulfanilamide and its derivatives. Domagk was born in Lagow, Germany, in 1895. His principal early work was in the field of pathology. After teaching at Greifswald and Muenster universities he became director in 1927 of the Institute of Experimental Pathology of the I. G. Dye Works in Elberfeld. Late in 1932 he first demonstrated the curative effects of prontosil (now neoprontosil) in the streptococcic infections of mice. After many careful observations, the details of the new discovery were finally published by Domagk in medical and scientific journals early in 1935. He had earlier received the Emil Fischer Medal, highest award of the German Chemical Society, in 1937 and the Cameron Prize of the University of Edinburgh in 1939.

RABIES

The study of rabies conducted by the International Health Division of the Rockefeller Foundation in cooperation with the Alabama State Board of Health already has been prosecuted to the point where the building program has been completed.[1] The total expenditures for public health work in this field have come to more than $108,000 for the four years 1935 to 1938 inclusive. Particular attention is being directed to a study of the efficacy of preventive measures in rabies. Alabama, with an estimated dog population of 450,000, vaccinated 220,000 dogs during 1937, the first year the compulsory law went into effect. During 1938, 134,000 dogs were vaccinated and nearly 18,000 killed as strays. Attempts have also been made to determine whether the rat plays a part in the spread of rabies, but so far experiments of this nature have been negative. All attempts to cultivate rabies street virus have been unsuccessful. A fixed strain obtained from the Alabama State Board of Health has been carried through sixty-eight transfers without difficulty. As yet it has been impossible to obtain growth on the chick embryo. A report on the effect of various diluents acting for short periods on the rabies virus in high dilutions has also been made. A fruitful outcome to these investigations would be of tremendous benefit to many portions of the country in which rabies remains endemic.

1. Annual report of International Health Division of the Rockefeller Foundation, 1938, p. 62.

CHRONIC LEUKEMIA

Because of the characteristic insidious onset of the leukemias they are usually first recognized only after widespread anatomic and physiologic abnormalities have developed. Wintrobe and Hasenbush [1] reviewed all cases of chronic leukemia in adults observed at the Johns Hopkins Hospital between January 1926 and August 1938, collecting thirty-nine cases of myelogenous and forty-seven cases of lymphogenous leukemia for study. Five of the patients who subsequently developed typical chronic myelogenous leukemia were found to have unexplained leukocytosis in the absence of typical leukemic signs or symptoms. The discovery was made in the course of routine examination following pregnancy in one case, for sterility in another, because of symptoms suggestive of disease of the gallbladder in the third, for abdominal distress in the fourth, and because of uterine myomas in the last. A reasonable estimate of the time elapsing from the onset of chronic myelogenous leukemia until symptoms of the disease commonly cause the patient to seek medical attention is probably from two to five years or longer. Data concerning the early phase of chronic lymphogenous leukemia were available in sixteen cases. The disease was first discovered in three men aged 59, 67 and 72 when examined for symptoms due to prostatic hypertrophy. Other patients were examined because of sugar in the urine, a psychoneurotic disorder and "indigestion." Unlike myelogenous leukemia, the finding of unexplained leukocytosis was the first evidence of the disease in only about one third of the cases of early lymphogenous leukemia. In another third, glandular enlargement was the sign which first attracted attention. The time interval between the observation of signs suggesting lymphogenous leukemia and the development of symptoms of the disease was from one and one-half to two and one-half years. The earlier recognition of lymphogenous leukemia, as compared with that of myelogenous leukemia, is explained, these authors believe, by the greater frequency with which glandular enlargement sufficient to attract attention occurred in the patents with the former. Males predominated in both groups. In 72 per cent of the cases of myelogenous leukemia the age of onset was between 30 and 59 years, while in 61.7 per cent of the cases of lymphogenous leukemia symptoms began between 50 and 69 years. In addition to the unexplained leukocytosis so frequent in early chronic myelogenous leukemia, distinct lymphocytosis was found commonly characteristic of early lymphogenous leukemia even when the leukocyte count was relatively low. Solution of potassium arsenite was without value in lymphogenous leukemia and of less value than irradiation in myelogenous leukemia. Response to irradiation was slightly better in myelogenous than in lymphogenous leukemia. Contrary to the frequently expressed opinion, infections in the majority of cases did not produce a remission in physical signs or the blood picture. Persistent unexplained leukocytosis must therefore be considered a premonitory sign of chronic myelogenous leukemia, and persons in whom it occurs should be carefully studied with that disease in mind.

1. Wintrobe, M. M., and Hasenbush, L. L.: Chronic Leukemia, Arch. Int. Med. **64**: 701 (Oct.) 1939.

ORGANIZATION SECTION

GRADUATE MEDICAL EDUCATION

A PROGRESS REPORT OF THE FIELD STUDY ON GRADUATE MEDICAL EDUCATION IN THE UNITED STATES BEING CONDUCTED BY THE COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

WASHINGTON

WASHINGTON STATE MEDICAL ASSOCIATION

On Aug. 30, 1939, the House of Delegates of the Washington State Medical Association resolved that a program for providing postgraduate medical education in the state of Washington be developed by the postgraduate medical education committee under the general supervision of the board of trustees. This committee, with Dr. Homer D. Dudley as chairman, has considered the postgraduate experiences of various state societies. On the basis of these studies the committee has recommended the following program:

1. Continuation of the graduate medical course for physicians throughout the state given annually in cooperation with the King County Medical Society and the Extension Division of the University of Washington with the additional assistance of the postgraduate committee of the state medical association, the association aiding in the arrangements and in publicity.

2. Inauguration of circuit courses by out of state lecturers under the supervision of the committee by providing defined lecture districts, securing competent speakers for a series of five days' instruction in each locality, including clinics, stressing subjects chosen by the physicians of each district, and by charging registration fees adequate to finance the regional program.

3. Provision of speakers from the membership of the state association to supplement the out of state lecturers. This will be made from a list compiled by the association. From the list component county medical societies may choose competent Washington physicians, and each society will be expected to finance their expenses.

4. Desirability of having other committees concerned with medical education consult with the committee. The postgraduate committee has emphasized this so that all postgraduate activities within the state may be properly correlated and coordinated.

The 1939 annual meeting of the Washington State Medical Association, held in Spokane, was devoted to graduate instruction. Five instructors from Washington University School of Medicine, St. Louis, were engaged in a cooperative agreement with the state medical associations of Oregon and Idaho. At the three day annual meeting, subjects discussed included cancer, chemotherapy, cholecystography, infant feeding, pneumonia, puerperal infection and toxemias of pregnancy. Attendance totaled 460 physicians. Of the 2,123 physicians in the state of Washington, 1,468 are members of the state medical association.

WASHINGTON STATE DEPARTMENT OF HEALTH

(Instruction in Obstetrics and Pediatrics)

Previous to 1938 the education program of the Washington State Department of Health for physicians practicing in the state had been carried on through itinerant child health conferences. It was proposed in 1938 that the itinerant conferences be held only as a means of introducing a clinic or of determining the need for a clinic in a given area, the educational program to consist largely of a refresher type of course by recognized authorities in obstetrics or pediatrics. An out of state physician and Washington physicians were to consider such subjects as endocrinology, internal medicine, nutrition and dental problems.

In May 1938 an out of state obstetrician gave three days of lectures and conferences in each of seven cities of the state. The committee on maternal and child welfare of the state medical association cooperated in sponsoring this program. A $2 registration fee was charged. The course of six lectures was attended by 217 physicians.

The chairman of the committee on maternal and child welfare, Dr. H. H. Skinner, recommended in 1938 that the committee membership be made permanent and that the committee be composed of an equal number of obstetricians and pediatricians serving overlapping five year terms.

In 1938 a committee of eight was formed as a permanent committee on medical cooperation and participation in the maternal and child hygiene program of the state department of health. On this committee were three representatives of the Washington sections of the North Pacific Pediatric Society, three of the Washington State Obstetrics Association and the director of the state department of health and the chief of the division of maternal and child hygiene. This committee now acts in an advisory capacity to the health department.

During May 1939 the division of maternal and child hygiene of the state department of health and the committee of eight jointly sponsored a three day series of afternoon and evening lectures in seven cities of Washington and in Vancouver, B. C. The assistance of county medical societies was enlisted in each locality and the secretaries were provided with post card announcements. An out of state medical school instructor gave six lectures on heart diseases, hemorrhage and toxemias of pregnancy, obstetric analgesia and cesarean sections in each center. Six hundred and thirteen physicians was the total attendance recorded. No registration fees were charged, since the state department of health provided financial support.

UNIVERSITY OF WASHINGTON

The University of Washington, Seattle, in cooperation with King County Medical Society, has conducted a five day graduate medical course during July each year since 1916. Dr. David C. Hall is executive secretary of the course and Dr. Raymond L. Zech was chairman of the county society committee of fourteen in 1939. There is also a committee of five staff members of the King County Hospital responsible for organizing clinical instruction. Every year four or more out of state physicians are engaged as a faculty, and in July 1939 five members of the faculty of Northwestern University Medical School, Chicago, and a member of the United States Public Health Service participated. Local physicians supplement the guest speakers by providing clinics. Instruction is scheduled from 9 a. m. to 10 p. m. daily. Major subjects of medicine are included and in case discussions two or three physicians participate, stressing the various approaches to the problems presented. Lectures are held on the university campus and clinics and demonstrations are given at the county hospital by members of the staff. Didactic lectures are limited to from forty to fifty minutes and clinics to from ten to twenty minutes. Medical and surgical clinics considered thirteen of the various specialties of surgery and three of the special subjects of medicine in 1939. Daily demonstrations were held in pathology, roentgenology and anesthesia as well as scientific exhibits in other subjects.

The extension division of the university aids in administering the course. A registration fee of $10 is charged which has provided sufficient support. Every physician in the state is sent a notice; announcements are published in *Northwest Medicine*. Annual attendance has ranged from 207 to 311 physicians.

LIBRARY SERVICE

The King County Medical Society, in addition to the active participation of its members in the annual graduate programs at the University of Washington, has provided library facilities for physicians practicing in the vicinity of Seattle. Space has been provided in the Cobb Building, Seattle, with adequate stacks and reading rooms. There are 11,468 volumes, three fifths of which are periodicals, a total of 233 being regularly

received. Ten dollars from the annual dues of every county society member supports the library. About two thirds of the members of the society used the library in 1938, as well as approximately 200 other physicians. The package lending service is available to individuals or to other libraries. Out of town physicians must supply postage. During 1938, 6,300 items were circulated.

Libraries with paid librarians are also maintained by the Spokane County Medical Society and the Pierce County Medical Society, the facilities being available to physicians practicing in the vicinity of Spokane and Tacoma.

OTHER GRADUATE ACTIVITIES

The Seattle Surgical Society provides a two day program each year. The Spokane Surgical Society, the Puget Sound Surgical Society and the Tacoma Surgical Society present annual graduate days. One or more guest speakers are provided to discuss cases presented by Washington physicians. Members of state medical associations are invited to attend. Registration fees vary from $2 to $3.

IDAHO

IDAHO STATE MEDICAL ASSOCIATION

At the September 1933 meeting of the House of Delegates of the Idaho State Medical Association, it was recommended by Dr. J. N. Davis that graduate study be considered and that the advisability and feasibility of securing members of medical school faculties for an annual continuation course be determined.

In September 1934 the house of delegates authorized the president of the state association, Dr. Charles R. Scott, to appoint a committee of six members to arrange a graduate course for the next annual meeting. Fifteen hundred dollars was the initial allocation for financing the state association's graduate program.

In planning the course of instruction certain principles were elaborated, since it was felt that the medical association had two primary obligations, first, to improve medical care and, second, to enlighten the public on personal and public health. It was decided that five days should be devoted each year to an integrated and correlated course of instruction in subjects of general interest selected on suggestions of physicians. Five instructors from a different medical school each year would organize as a traveling faculty, thus providing a harmonized course. Each day five or six fifty minute lectures would be scheduled with additional round table discussions.

The state association has assumed responsibility for financing its graduate program. In 1936, when the constitution and by-laws of the association were modified, the Idaho Medical Foundation was established with the members of the council as trustees of the foundation. A foundation fund of $10,500 was established by contributions from members of the state association which constituted a percentage of fees which they had received for the care of special groups of patients. The income from the foundation's funds is available for financing graduate activities. This has not been necessary, however, since registration fees of $5 or $10 have been sufficient to meet each year's expenses. Each speaker is given an honorarium and his traveling expenses.

The committee on scientific work of the state association is a standing committee consisting of three members, one selected each year to serve three years. The present chairman of this committee is Dr. C. W. Pond. Ex officio members are the president and the secretary-treasurer of the association. The secretary acts with the committee on scientific work in arranging the annual graduate program.

Beginning in 1935 a traveling faculty from the following medical schools has participated each year: Northwestern University Medical School, University of California Medical School, University of Minnesota Medical School, University of Michigan Medical School and Washington University School of Medicine. In 1937 Idaho physicians presented clinical cases for discussion in local hospitals to supplement the faculty lectures. Attendance has varied from 116 to 144. Of the 406 physicians in Idaho, 272 are members of the state association.

IDAHO STATE DIVISION OF PUBLIC HEALTH

In November 1936 the Idaho State Division of Public Health, in cooperation with the Idaho State Medical Association, conducted an itinerant postgraduate lecture course in six cities of the state. Three out of state physicians participated in the one and two day afternoon and evening sessions in obstetrics and pediatrics. The chairman of the state association's committee on scientific work arranged the program and selected the speakers. The county medical society in each locality arranged the details for each meeting. The course was attended by 181 physicians; no registration fees were charged. The health division financed this effort.

During 1937 instruction in pediatrics was provided in two cities of the state by one out of state physician. Attendance at these lectures approximated seventy-five.

In April and May 1938 four out of state physicians conducted a postgraduate course in pediatrics, dermatology and syphilology and orthopedics in five cities of the state. One day sessions were held in four places and two days were allowed in a fifth. Meetings were held in hotels and in two cities; clinical demonstrations were attempted. Approximately 150 physicians attended the 1938 itinerant course.

Lectures in syphilology, pediatrics, orthopedics and general medicine were given in the spring of 1939. Three out of state physicians participated in one day meetings held in five localities. One hundred and seventy physicians enrolled. No registration fees were charged.

IDAHO ANTI-TUBERCULOSIS ASSOCIATION

During the past two years the Idaho Anti-Tuberculosis Association has offered a consultation service to practicing physicians of the state in the interpretation of roentgenograms. The consultant also participates in the activities of the state division of public health.

OREGON

OREGON STATE MEDICAL SOCIETY

At the 1939 annual meeting of the Oregon State Medical Society three out of state faculty members who had participated in the annual meetings in Idaho and Washington took part in the scientific program. A fourth guest speaker was also included. This enabled the committee on scientific work to provide members of the association with an integrated general course of twelve lectures in pediatrics, obstetrics, surgery and medicine. Round table discussions were held and twenty-four contributions were made by Oregon physicians on other subjects. The three and one-half day session was devoted substantially to postgraduate instruction and, by the cooperative agreement with the medical societies of two adjoining states, it was possible to present a comprehensive and instructive program. There are 805 members of the Oregon State Medical Society of the 1,386 physicians in the state.

At the June 1939 meeting of the council of the state medical society the president of the society, Dr. Charles E. Sears, was authorized to appoint a committee on postgraduate medical education. Dr. Karl H. Martzloff was made chairman of a committee of five members. This committee met in September 1939 to discuss the establishment of a graduate program.

The Oregon State Medical Society, in cooperation with the Oregon State Board of Health, provided one or two days of lectures in obstetrics and pediatrics in nine cities of the state this year. The committee on maternal welfare, Dr. Raymond Watkins, chairman, with the director of the division of maternal and child health, Dr. G. D. Carlyle Thompson, arranged the lecture series for May 1939. Each component medical society which participated selected topics from a list of twelve subjects outlined by the out of state obstetrician and pediatrician engaged to give the instruction. From six to ten afternoon and evening lectures were held in each center, except one in which the instruction began at 9 a. m. Two hundred and seventy-seven physicians from twenty-one counties enrolled. No registration fees were charged, since the program was supported by federal funds.

The Oregon Academy of Ophthalmology and Otolaryngology and the University of Oregon Medical School have provided a week of lectures and clinics at Portland for ophthalmologists and otolaryngologists over the past four years. While the course is primarily intended for physicians in special practice, subjects of general interest to practicing physicians are included. Surgical anatomy of the head and neck is demonstrated at the medical school and two out of state speakers present didactic

instruction. This is followed by round table discussions and outpatient clinical exercises. A registration fee of $25 is charged. The average number of physicians attending is sixty.

The University of Oregon Medical School has developed a traveling clinic under its child guidance program and during 1937-1938 established thirteen centers over the state. Teams consisting of three instructors from the medical school have constituted the staff of this traveling clinic and when a district was visited these instructors were available for discussions and demonstrations before the local medical society.

The University of Oregon Medical School provides library facilities for practicing physicians. During 1938-1939, 499 Oregon physicians and thirty-eight physicians from other states made use of the library.

OFFICIAL NOTES

ADDRESSES BY OFFICIAL STAFF

DR. W. W. BAUER:

November 8—Public Health Meeting, Springfield, Mass.
November 16—Rush Medical College, Senior Students, Chicago.
November 28—Chicago Control of the Controllers Institute of America, Chicago.

DR. MORRIS FISHBEIN:

November 7—Tufts Medical School, Boston.
November 7—Greater Boston Medical Society, Boston.
November 8—Association for Advancement of Industrial Medicine and Surgery, New York.
November 9—Essex County Medical Society, Newark, N. J.
November 10—Hudson County Medical Society, Jersey City, N. J.
November 14—Northwestern University School of Journalism, Evanston, Ill.
November 21—Central Lions Club, Chicago.
November 28—Public Affairs Group, Chamber of Commerce, Omaha.
November 28—University of Nebraska College of Medicine, Omaha.
November 28—Creighton University School of Medicine, Omaha.
November 28—Omaha-Douglas County Medical Society, Omaha.
November 30—Rush Medical College, Chicago.

DR. EDWIN P. JORDAN:

November 17—Woman's Auxiliary, Aux Plains Branch, Chicago Medical Society, Chicago.

DR. R. G. LELAND:

November 21—Lake View High School Civic Forum, Chicago.

DR. ROCK SLEYSTER:

November 10—Woman's Auxiliary to the Medical Society of Milwaukee County, Milwaukee.
November 16—County Medical Society, Springfield, Ill.
November 22—Southern Medical Association, Memphis, Tenn.

DR. PAUL A. TESCHNER:

November 6—North Shore Branch, Woman's Auxiliary of the Chicago Medical Society, Chicago.
November 8—George Williams College, Chicago.
November 16—Marion County Tuberculosis Association, Indianapolis.
November 21—West School Parent Teacher Association, Des Plaines, Ill.

DR. NATHAN B. VAN ETTEN:

November 11—The Pittsburgh Academy of Medicine, Pittsburgh.

"BOOTLEG" AUTOMOBILE EMBLEMS

Years ago the American Medical Association had copyrighted the design used on the official A. M. A. auto emblem. The design comprised essentially the Aesculapian (knotty) rod entwined by one serpent placed on the center of a green cross, with the letters M.D. beside the rod. The use of this official emblem has been restricted to members of the American Medical Association and thousands of the emblems have been manufactured and distributed in this way to be placed on physicians' cars, sometimes including also the name of the constituent society of which the physician is also a member. Several imitations or bootleg auto emblems have since appeared on the market. The design used by the imitators is different, comprising a straight rod with wings at the top and entwined by two serpents. The bootleg emblem is distributed by unofficial agencies who make no effort to determine that purchasers are physicians. Members of the American Medical Association should beware of imitation emblems. The official auto emblem bears a serial number in the small panel, which is registered at the headquarters of the American Medical Association with the name of the user and thus becomes an authoritative means of establishing one's identity in troublesome traffic situations. Keen observers can readily distinguish between the official emblem and bootleg auto emblems.

WOMAN'S AUXILIARY

ANNUAL MEETINGS

Mrs. Rollo K. Packard, president of the Woman's Auxiliary to the American Medical Association, addressed annual meetings of auxiliaries to the following state medical societies: Kentucky at Bowling Green September 13, Michigan at Grand Rapids September 19, Pennsylvania at Pittsburgh October 2, Virginia at Richmond October 4 and Delaware at Wilmington October 10.

The annual meeting of the auxiliary to the Indiana State Medical Association was held in Fort Wayne October 10-12. Mrs. Maurice B. Van Cleave is the retiring president.

The annual meeting of the auxiliary to the State Medical Society of Wisconsin was held in Milwaukee September 12-14. Dr. Rock Sleyster, President of the American Medical Association, addressed the auxiliary. Mrs. Robert E. Fitzgerald is the retiring president and Mrs. Frank W. Pope is president 1939-1940.

The annual meeting of the auxiliary to the Utah State Medical Association was held in Salt Lake City, September 5-7, during the time of the meeting of the Rocky Mountain Medical Conference. Speakers at the meeting were: Dr. Claude L. Shields, president of the Utah State Medical Association; Dr. E. M. Neher, chairman of the advisory council to the auxiliary; Dr. J. W. Aird, the oldest physician in the practice of medicine in Utah, and Dr. Edward Jackson, guest speaker from Denver. Mrs. W. M. Stookey, retiring president, presided. Mrs. J. J. Weight, Provo, is president 1939-1940.

Mississippi

Northeast Mississippi Thirteen Counties Auxiliary met in Aberdeen September 12. Mrs. V. B. Philpot is president of this group. Dr. W. H. Anderson, Boonville, president-elect of the Mississippi State Medical Association and editor of the *Mississippi Doctor*, spoke, presenting the objective of the state medical association. The auxiliary will assist the association in its program of securing satisfactory legislation on vital statistics, food and drugs, an antibarbituric acid law and the revision of the mortmain law, which at present forbids bequests of property to orphanages, hospitals, colleges and the like which are related to a church. Mrs. Hugh H. Johnston, president, reports a membership of 312.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ARKANSAS

First Full Time Professor of Medicine.—Dr. Raymond L. Gregory, professor of medicine at Howard University College of Medicine, Washington, D. C., has been appointed professor and head of the department of medicine at the University of Arkansas School of Medicine, Little Rock, newspapers report. This is said to be the first full time appointment to the position. Dr. Gregory graduated at the University of Minnesota Medical School in 1929 and has served on the faculties of the medical schools of the University of Iowa and Louisiana University. He has been associated with Howard since 1937. Dr. Silas C. Fulmer has been professor of medicine at the University of Arkansas and acting part time head of the department.

CALIFORNIA

Society News.—The staff of Providence Hospital presented the following program before the Alameda County Medical Association in Oakland October 16: Drs. Philip J. Dick, "Rectal Polyps"; Malcolm B. Hadden, "Russell Traction and Treatment of Fractured Femurs"; Robert S. Peers, "Gout and Arthritis — Differential Diagnosis," and Lester B. Lawrence, "Intraspinal Tumors—Comments on Diagnosis."——At a meeting of the Los Angeles Surgical Society October 13 Drs. Rupert B. Raney spoke on "Complications of Craniocerebral Trauma Benefited by Surgery" and Mark A. Glaser, "A New Regime for Treatment of Head Injuries."——A symposium on sulfanilamide and sulfapyridine was presented before the San Francisco County Medical Society October 10 by Drs. Arthur Haim, Dwight L. Wilbur, Donald A. Dallas, Edward B. Shaw, Thomas E. Gibson and Jesse L. Carr. —— The San Mateo County Medical Society was addressed in San Mateo October 25 by Drs. Mayo H. Soley and Paul A. Gliebe, both of San Francisco, on "Physiologic Syndromes Which Simulate Organic Disease."

Railway Surgeons' Meeting.—The thirty-seventh annual convention of the Pacific Association of Railway Surgeons was held at the Clift Hotel, San Francisco, September 29-30 with the following speakers among others:

Dr. Lionel D. Prince, San Francisco, A Method of Treatment of Fractures of the Patella.
Dr. Ralph M. L. Dodson, Portland, Ore., Fractures of the Transverse Processes of the Lumbar Vertebrae.
Dr. Howard A. Brown, San Francisco, The Neurologic Aspects of Low Back Pain and Sciatica.
Dr. Leo L. Stanley, San Quentin, Testicular Substance Implantation.
Dr. Charles R. L. Mathe and Robley C. Archambeault, M.A., San Francisco, Spectrographic Analysis of Urinary Calculi: A Preliminary Report.
Dr. Edward M. Butt, Los Angeles, Virus Infections.
Dr. Eugene S. Kilgore, San Francisco, The Management of Coronary Disease in Engineers.
Dr. Grant L. Selfridge, San Francisco, Deafness.
Drs. Charles A. Thomas and Stirley C. Davis, both of Tucson, Ariz., Tuberculosis in the Aged.
Dr. Edmund J. Morrissey, San Francisco, A New Test for Circulatory Disturbances in the Hand.
Dr. Lloyd B. Crow, San Francisco, Roentgenologic Demonstration.

Dr. Richard J. Flamson Jr., Los Angeles, gave the presidential address on "The Status of the Railway Surgeon."

FLORIDA

East Coast Meeting.—The Florida East Coast Medical Association will hold its annual meeting at Ponte Vedra November 10-11. The speakers will include:

Dr. Clarence Larimore Perry, Miami, Differential Diagnosis and Treatment of Vulvar Granuloma Inguinale.
Dr. Claude Anderson, Orlando, Intrathoracic Goiter or Adenoma of the Thyroid.
Dr. Isaac M. Hay, Melbourne, Endometriosis.
Dr. Eugene L. Jewett, Orlando, Fractures of the Femur.
Dr. James C. Nowling, West Palm Beach, Acute Meningitis Caused by Influenza Bacillus.
Dr. James J. Nugent, Miami, Pyelonephritis—Recent Improvements in Treatment.

A symposium on management of chest tumors will be presented by Drs. Louie M. Limbaugh, Raymond H. King, Wilfred McL. Shaw and Kenneth A. Morris. All are from Jacksonville. Dr. Frank K. Boland, Atlanta, Ga., will be the guest speaker at this meeting.

ILLINOIS

Free Pneumonia Serum and Sulfapyridine.—The state department of health announces that during the current pneumonia season both serum and sulfapyridine will be distributed free. To obtain them, physicians must have specimens from patients tested in approved laboratories for the type of pneumonia involved and must agree to render reports to the department. Deaths occurred at the rate of 94 per thousand among serum-treated patients against 150 per thousand among comparable nonserum-treated patients during the first half of 1939. These two groups were all from a list of 2,100 patients from whom specimens were taken and tested in approved laboratories. The serum and sulfapyridine may be obtained from the centers which have been established throughout the state.

Chicago

Personal. — Miss Alice H. Miller, Gainesville, Fla., has been appointed director of public health for the Tuberculosis Institute of Chicago and Cook County, succeeding Mrs. Adelaide Ross, resigned.

Koessler Fellowship Awarded.—Dr. James J. Smith, St. Louis University School of Medicine, class of 1937, has been awarded the Jessie Horton Koessler Fellowship of the Institute of Medicine of Chicago. Under the fellowship, which carries a stipend of $500, Dr. Smith will work with Dr. Andrew C. Ivy at Northwestern University Medical School in research on evacuation of the gallbladder in pregnancy.

Ophthalmology for General Practitioners.—The Illinois Eye and Ear Infirmary announces that a course in refraction and diseases of the eye will be offered during the week of December 4 for general practitioners in towns outside of Cook County and not nearer than 25 miles to an ophthalmologist. The course will be limited to six men and the fee will be $25. Information may be obtained from the dean of instruction, Illinois Eye and Ear Infirmary, 904 West Adams Street.

Society News.—The Chicago Society of Internal Medicine will be addressed November 27 by Drs. Michael H. Streicher on "Appendicitis—Incidence of Amebiasis in a Clinical Review of 3,407 Cases"; Ralph B. Bettman and Gemma M. Lichtenstein, "Acute Cholecystitis" and Laurence E. Hines, Allen H. Hoover and Edwin C. Graf, "Effect of Sulfanilamide on the Fibrinolytic Activity of Hemolytic Streptococci."——The Chicago Laryngological and Otological Society will be addressed November 6 by Drs. Hans Brunner on "Surgical Repair of Facial Paralysis"; Frank J. Novak Jr., "Giant Follicular Hypertrophy of Nasopharynx," and William A. Smiley, "Subglottic Polyp Following Intratracheal Anesthesia."

Symposium on Nutritional Deficiency. — The Chicago Medical Society will sponsor a symposium on nutritional deficiency at Thorne Hall, Northwestern University Medical School, November 15 with the following speakers: Dr. Tom D. Spies, Cincinnati; Dr. Frederick T. Jung, Smith Freeman, Ph.D., Dr. Warren H. Cole, Chester J. Farmer, A.M., Drs. Arthur F. Abt, Don C. Sutton, John Ashworth, Nathan S. Davis III, Edward D. Allen, Bengt L. K. Hamilton, Howard L. Alt, Charles B. Puestow and Clifford J. Barborka and Franklin C. Bing, Ph.D. The symposium will begin at 9 o'clock in the morning, and in the evening following dinner at the Chicago Woman's Club Dr. Spies will discuss "Vitamin B and Pellagra."

INDIANA

State Medical Election.—Dr. Albert M. Mitchell, Terre Haute, was chosen president-elect of the Indiana State Medical Association at its annual meeting in Fort Wayne October 12. He will take office in January 1941. Dr. Karl R. Ruddell, Indianapolis, will be inducted into the presidency in January 1940. The 1940 session of the association will be held in French Lick.

Society News. — The Fort Wayne Medical Society was addressed recently by Dr. Richard W. Terrill, Fort Wayne, on "Treatment of Foreign Bodies in the Eye."——At a meeting of the Montgomery County Medical Society in Crawfordsville September 21 Dr. George S. Bond, Indianapolis, discussed coronary disease. —— Dr. Arthur N. Ferguson, Fort Wayne, spoke on heart disease at a recent meeting of the Whitley County Medical Society in Columbia City.

District Meeting.—The sixty-second semiannual meeting of the Eleventh Indiana Councilor District Medical Association was held at Marion October 18. In the morning Dr. Quitman U. Newell, professor of clinical obstetrics and gynecology, Washington University School of Medicine, St. Louis, conducted a clinic and in the afternoon the following spoke: Drs. Cyrus J. Clark, Indianapolis, "Sulfapyridine and Allied

Therapy in Treatment of Pneumonia"; Charles L. Wise, Camden, "Is Convalescent Serum of Value?" and Carl P. Huber, Indianapolis, "Recent Trends in the Investigation and Treatment of Sterility." Dr. Newell addressed the banquet session in the evening.

KANSAS

New Health Director for Kansas City.—Dr. Ragnar T. Westman, formerly health officer of Bay County, Mich., has been appointed city health director of Kansas City, succeeding the late Dr. William F. Lunsford. Dr. Westman graduated at the University of Minnesota Medical School, Minneapolis, in 1931. He formerly served as chief quarantine officer of Minneapolis.

Postgraduate Courses.—Two postgraduate courses on obstetrics and pediatrics began in various sections of south central and southeastern Kansas October 23 to continue through November 17. The speakers are Drs. John H. Randall and William F. Mengert, State University of Iowa College of Medicine, Iowa City; Morris Edward Davis and William J. Dieckmann, Department of Medicine of the Division of Biological Sciences, University of Chicago; Mandel L. Spivek of the Children's Memorial Hospital, Chicago, and Julian D. Boyd, associate professor of pediatrics at Iowa.

LOUISIANA

Society News.—At the joint scientific and third quarterly executive meeting of the Orleans Parish Medical Society October 9 Dr. Earl Conway Smith discussed treatment of trichomonas vaginalis vaginitis; Dr. Rufus H. Alldredge, "Fractures of the Humerus," and Dr. Donovan C. Browne, "Gastroscopy—Its Relation to Surgery." All are of New Orleans.

Personal.—Dr. Erasmus D. Fenner, New Orleans, has presented to the library of the school of medicine of Louisiana State University a collection of medical books and journals from his library.——Dr. Edgar Hull, assistant professor of medicine, Louisiana University Medical Center, New Orleans, has been appointed acting head of the department of medicine, to succeed the late Dr. George S. Bel.

Dr. Tripoli Appointed Professor.—Dr. Carlo J. Tripoli has been appointed professor of medicine in charge of the department of medicine of the Graduate School of Louisiana State University, New Orleans. A graduate of Tulane University of Louisiana School of Medicine, New Orleans, class of 1929, Dr. Tripoli has been serving on the staff of the state university since 1931; he has been assistant professor of medicine since 1938. He is also chairman of the section on medicine of the state medical society.

MASSACHUSETTS

Dr. Schall to Succeed Dr. Mosher.—Dr. Leroy A. Schall, instructor in laryngology, Courses for Graduates, Harvard Medical School, Boston, has been promoted to the position of Walter Augustus Lecompte professor of otology and professor of laryngology, succeeding Dr. Harris P. Mosher, who becomes professor emeritus. Dr. Schall graduated at Jefferson Medical College of Philadelphia in 1917. He has served as surgeon in otolaryngology at the Massachusetts Eye and Ear Infirmary; vice chairman of the Section on Laryngology, Otology and Rhinology, American Medical Association, Chicago, 1936-1937, and secretary from 1937 to 1939. Dr. Mosher has for many years been president of the American Board of Otolaryngology. He was chairman of the Section on Laryngology, Otology and Rhinology of the American Medical Association for the year 1932-1933 and president of the American Academy of Ophthalmology and Otolaryngology in 1929.

Clinical Conference on Physical Medicine.—The New England Society of Physical Medicine will hold a clinical conference at the Hotel Kenmore, Boston, November 8-9 with a special session at the Massachusetts Institute of Technology the morning of November 10. The speakers will include:

Dr. Harold E. Himwich, Albany, N. Y., Nitrogen Therapy: Physiologic Aspects in Schizophrenia.
Drs. Charles W. McClure and Isaac R. Jankelson, Boston, Gastroscopy.
Dr. Temple S. Fay, Philadelphia, Observations on Human Refrigeration.
Dr. William H. Schmidt, Philadelphia, Surgical Diathermy.
George R. Harrison, Ph.D., Cambridge, Mass., Modern Physics and the Modern Physician.
Harold E. Edgerton, Sc.D., Cambridge, Seeing the Unseen with Stroboscopic Photography.
Dr. Edward A. Edwards, Boston, and Seibert Q. Duntley, Sc.D., Cambridge, The Pigments and Color of Living Human Skin.
Dr. Rebekah Wright, Boston, Hydriatic Sedatives.

The program also includes symposiums and demonstrations covering a wide range of subjects in the field of physical medicine. For the special session at Massachusetts Institute of Technology the lecturers will be: Joseph W. Horton, Sc.D., associate professor of biologic engineering; Arthur C. Hardy, Sc.D., professor of optics and photography; Robley D. Evans, Ph.D., associate professor of physics, and John G. Trump, Sc.D., assistant professor of electrical engineering.

MICHIGAN

Urologists Observe Anniversary.—The Detroit branch of the American Urological Association celebrated its twenty-fifth anniversary October 12. The fifty-one members present inscribed their names on a plaque to be forwarded to Dr. Frederick W. Robbins, formerly of Detroit and now of Pasadena, Calif., who in 1914 secured the charter from the American Urological Association.

MINNESOTA

Pilgrimage in Honor of Doctors Mayo.—In response to the request of many members, the council of the Minnesota State Medical Association sponsored a memorial pilgrimage to Rochester October 27 to pay tribute to Drs. William J. and Charles H. Mayo. Every member of the association was invited to participate in the ceremonies at Plummer Hall in the Mayo Clinic and at Oakwood Cemetery. With Dr. George A. Earl, St. Paul, president of the state medical association, presiding, at the memorial meeting in Plummer Hall Dr. Edward L. Tuohy, Duluth, gave the address entitled "An Expression from the Medical Profession of Minnesota." There followed a procession to the cemetery.

Society News.—The Minnesota Pathological Society was addressed October 12 by Dr. George H. Whipple, Rochester, N. Y., on "Production, Utilization and Significance of Blood Proteins."——Dr. Perrin H. Long, Baltimore, delivered a Mayo Foundation lecture October 10 in Rochester on "Experimental and Clinical Use of Sulfapyridine and Its Sodium Derivative in Treatment of Pneumococcal Infections."——At the seventy-first annual meeting of the Wabasha County Medical Society in Lake City October 5 Dr. Bertram J. Bouquet, Wabasha, delivered the presidential address on "Malaria with Case Report." Other speakers included Drs. Philip H. Heersema, Rochester, on "Tetanus and Its Prevention"; Robert A. Glabe, Plainview, "Surgical Drainage of the Abdomen," and William E. Bannen, La Crosse, Wis., "Urologic Pathologic Museum."——Dr. Robert M. Burns, St. Paul, discussed "Accidents in Homes and Industries" before the Washington County Medical Society recently.

NEW HAMPSHIRE

Restrict Sale of Vitamin Concentrates.—The state board of health has given notice to "cut-rate stores, department stores, groceries, etc," that sales of vitamin concentrates will render them liable to prosecution. These drugs fall in the category of potent drugs as defined by law and hence their sale by other than drugstores is deemed a violation. The concentrates are commonly in the form of small capsules, the contents of which are usually less than 60 minims (4 cc.).

NEW JERSEY

Society News.—Dr. Norman H. Plummer, New York, addressed the Morris County Medical Society, Greystone Park, Morris Plains, October 19 on "Treatment of Pneumonia."——Dr. Morris Fishbein, Chicago, Editor of THE JOURNAL, will address the Essex County Medical Society, Newark, November 9 on "American Medicine and the National Government."

NEW YORK

Society News.—Dr. Henricus J. Stander, New York, addressed the Medical Society of the County of Albany October 18 on "General Considerations of the Toxemias of Pregnancy."——Dr. William C. Clarke, Cornwall Bridge, Conn., addressed the Dutchess County Medical Society, Poughkeepsie, October 18 on "History of Surgery for the Past 200 Years," and Dr. Paul D. Keller, Brooklyn, discussed the "three cents a day plan."——Dr. Milton A. Carvalho, Binghamton, addressed the Broome County Medical Society, Binghamton, October 10 on "Use of the Cystogram in Diagnosis of Placenta Praevia."——At a meeting of the Seneca County Medical Society at Willard October 11 a symposium on arthritis was presented by Drs. Louis M. Lockie, Buffalo; Roscoe D. Severance, Syracuse, and Thomas W. Maloney, Geneva.

Cancer Advisory Committee Appointed.—The state health commissioner, Dr. Edward S. Godfrey Jr., Albany, has appointed an advisory committee to assist the new division of cancer control in outlining policies and make available to it

the specialized knowledge of the members. The committee consists of Drs. Robert S. Cunningham, dean, Albany Medical College, Albany; James Ewing, director, Memorial Hospital, New York; Thomas P. Farmer, Syracuse, chairman of the council committee on public health and education, Medical Society of the State of New York; John J. Morton Jr., surgeon in chief, Strong Memorial Hospital, Rochester, and Francis Carter Wood, professor of cancer research, Columbia University College of Physicians and Surgeons. Dr. Morton L. Levin, New York, has been appointed assistant director of the new division, which has set up headquarters in the New York State Teachers' Association building, Albany. Formation of the division was announced in THE JOURNAL, October 21, page 1575.

New York City

Second Harvey Lecture.—Conrad A. Elvehjem, Ph.D., professor of agricultural chemistry, University of Wisconsin College of Agriculture, Madison, will deliver the second Harvey Society Lecture of the season at the New York Academy of Medicine November 16. Dr. Elvehjem will speak on "The Biological Significance of Nicotinic Acid."

Conference on Convalescent Care.—The New York Academy of Medicine is sponsoring a conference on convalescent care November 9-10. The program will include the following subjects: physiology and psychology of convalescence, relation of chronic disease to convalescence, results of recent research in nutrition with particular reference to the convalescent state, institutional care for various types of patients, psychosomatic factors of convalescence and the socioeconomic aspects of convalescent care. In addition to the New York physicians who will present topics for discussion, the following guest speakers will participate: Drs. Oliver H. Perry Pepper and Isidor S. Ravdin, Philadelphia; William S. McCann, Rochester; Waldo E. Nelson, Cincinnati; Lewellys F. Barker and G. Canby Robinson, Baltimore. A general meeting will be held Friday evening November 10 at which the speakers will be Dr. I. Ogden Woodruff, E. H. Lewinski Corwin, Ph.D., and Mr. Alfred H. Schoellkopf.

NORTH CAROLINA

Society Adopts Farm Security Program.—The Johnston County Medical Society at a meeting October 10 adopted the Farm Security Administration program for medical care for 1940. The supervisory board will be composed of the president and secretary of the society and one other member appointed each year by the two officers. It was also voted to place *Hygeia* in all county schools at the expense of the society.

Special Society Meeting.—The fifth annual meeting of the North Carolina Eye, Ear, Nose and Throat Society was held in Statesville September 21. The guest speakers were Drs. John J. Shea, Memphis, Tenn., on "Prevention of Complications of the Surgery of Tonsils and Adenoids" and "Management of Fractures of the Facial Bones" and James W. White, New York, "Relation of Ocular Muscles and Refraction." Dr. Albert G. Woodard, Goldsboro, was elected president; Dr. Milton B. Clayton, Statesville, vice president, and Dr. Milton R. Gibson, Raleigh, secretary, reelected.

NORTH DAKOTA

Semiannual Special Society Meeting.—Dr. Lawrence M. Randall, Rochester, Minn., was the guest speaker at the semiannual meeting of the North Dakota Society of Obstetrics and Gynecology in Grand Forks October 21. His subject was "Some Clinical Phases of Endocrinology." Other speakers were Drs. James F. Hanna, Fargo, on "A Fifteen Year Review of Carcinoma of the Cervix Uteri at St. John's Hospital, Fargo"; John D. Graham, Devils Lake, "Medical Induction of Labor Near Term," and H. Robert Ransom, Grand Forks, "Pyelitis of Pregnancy."

OHIO

Annual Cardiovascular Institute.—The sixth annual cardiovascular institute under the auspices of the Heart Council of Greater Cincinnati, the West Virginia Heart Association and the Academy of Medicine of Cincinnati will be held November 14. The morning session will be at the Cincinnati General Hospital with Dr. William M. Sheppe, Wheeling, W. Va., speaking on "Syphilis of the Heart and Aorta" and Dr. Marion A. Blankenhorn, Cincinnati, "Hypertensive Heart Disease," and discussion by Dr. Timothy Leary, emeritus professor of pathology, bacteriology and medical jurisprudence, Tufts College Medical School, Boston. In the afternoon session at the University of Cincinnati College of Medicine Drs. Oscar B. Biern, Huntington, W. Va., and Johnson McGuire, Cincinnati, will conduct round table discussions on cardiovascular syphilis. In the evening Dr. Leary will deliver the first Alfred Friedlander Lecture at the Academy of Medicine on "Pathology of Syphilis of the Cardiovascular System."

PENNSYLVANIA

Society News.—Dr. David M. Davis, Philadelphia, spoke before the Lycoming County Medical Society in Williamsport October 13 on urinary infections in females.——Dr. Russell Richardson, Philadelphia, discussed "Advances in the Treatment of Diabetes" before the Cambria County Medical Society, Johnstown, October 12.——Drs. Howard J. Thomas, Greensburg, and Robert C. Johnston, New Kensington, addressed the Westmoreland County Medical Society at the Mountain View Hotel October 25 on "Toxemias of Pregnancy" and "Surgical Headaches" respectively.——Dr. Stanford W. Mulholland, Philadelphia, addressed the Delaware County Medical Society, Chester, October 12 on "Hypertension's Challenge to Urology."

Philadelphia

Society News.—Drs. Michael Scott and Hershel C. Lennon, among others, addressed the Philadelphia Neurological Society October 27 on "Decerebrate Tonic Extensor Convulsions as a Sign of Occlusion of the Basilar Artery."——A panel discussion of "Practical Orthopedics for the Pediatrist" was presented at a meeting of the Philadelphia Pediatric Society October 10 by Drs. DeForest P. Willard, John A. Brooke, Jesse T. Nicholson and John P. Scott.

The "Blockley" Dinner.—The Association of Ex-Resident and Resident Physicians of the Philadelphia General Hospital, for many years known as "Blockley," will hold its fifty-third annual dinner at the Bellevue-Stratford Hotel December 5. Dr. William S. Middleton, dean, University of Wisconsin Medical School, Madison, will be the guest of honor and Dr. Arthur C. Morgan, president of the association, will preside. Members who do not receive notices are requested to send their correct addresses to the secretary, Dr. George Wilson, 133 South Thirty-Sixth Street, Philadelphia.

Woman's Hospital to Celebrate Merger.—A day of scientific meetings in celebration of the tenth anniversary of the merger of the Woman's Hospital of Philadelphia and West Philadelphia Hospital for Women will be held December 1 for all who have served as interns and residents at either institution. In the morning Dr. Margaret C. Sturgis will conduct an operative gynecologic clinic and Dr. Mary Hoskins Easby a cardiac clinic, and Dr. Alberta Peltz will speak on "The Philadelphia Maternal Welfare Committee and Its Work." At the afternoon session the speakers will be Drs. Emily Lois Van Loon on "Bronchoscopy and Esophagoscopy as Related to the General Practitioner"; Emily P. Bacon, "Disorders in the Preschool Child," and Drs. Berta M. Meine and Ursula M. E. Hober, "Obstetric Service of the Woman's Hospital for the Past Ten Years," with demonstration. There will be a dinner in the evening at the Penn Athletic Club at which Dr. Mary R. H. Lewis, medical director of the hospital, will be toastmistress.

Pittsburgh

Society News.—At a meeting of the Allegheny County Medical Society October 17 the speakers were Drs. James W. Stevenson, Mount Lebanon, Pa., on "Bicornate Uterus Associated with Pregnancy"; Joseph W. Hampsey, "Masking of Clinical Picture of Acute Mastoiditis During the Administration of Sulfanilamide"; Alfred B. Sigmann, Bridgeville, "Clinical Study of Treatment, by Intra-Abdominal Lavage with 70 per Cent Alcohol, of Acute Suppurative Peritonitis (Appendiceal)," and Kenneth D. Eskey, "Sulfanilamide in Treatment of Gonorrhea."

VIRGINIA

Society News.—A symposium on pyloric stenosis was presented before the Mid-Tidewater Medical Society at Saluda recently by Drs. Nowell D. Nelms, Mathews; Russell von L. Buxton and William W. Falkener, Newport News; William Lowndes Peple and Charles R. Robins, Richmond.

Personal.—Dr. Leonard H. Denny has resigned as director of the department of public welfare of Portsmouth in order to return to service in the U. S. Navy, it is reported. Dr. Julian T. Miller, retired naval officer, has been appointed to succeed Dr. Denny.——Dr. William D. Tillson, director of the bureau of industrial hygiene, state department of health, since July 1936, has resigned to become medical director of the American Viscose Company, Parkersburg, W. Va.

State Medical Election.—Dr. Walter B. Martin, Norfolk, was named president-elect of the Medical Society of Virginia at the annual meeting in Richmond October 4 and Dr. Hugh

H. Trout, Roanoke, was installed as president. Vice presidents elected were Drs. Karl S. Blackwell, Richmond; Frank A. Farmer, Roanoke, and Philip W. Boyd, Winchester. Miss Agnes V. Edwards, Richmond, was reelected executive secretary-treasurer.

WASHINGTON

State Obstetric Meeting.—Dr. William M. Wilson, Portland, Ore., was the guest speaker at the annual meeting of the Washington State Obstetrical Society in Everett October 7. Dr. Wilson summarized discussions at the morning sessions and delivered two addresses, one at the afternoon session on "Experience with the Newer Endocrine Products" and another at the evening session on "Treatment of Pruritus Vulvae."

Society News.—Dr. Arthur E. Lien, Spokane, addressed the Spokane County Medical Society, Spokane, October 12 on "Nutrition and Its Relation to the Public Health."——The King County Medical Society was addressed October 16 by Drs. David Metheny on "Carcinoma of the Stomach" and Otis F. Lamson, Seattle, "Multiple Primary Carcinoma." Dr. Frank J. Heck, Rochester, Minn., addressed the society October 25 on "Practical Aspects of the Treatment of Anemia." A motion picture was shown on "The Adequate Neurological Examination" by Drs. Laurence Selling and Roger H. Keane, Portland, Ore.

WISCONSIN

Personal.—Dr. Virginia Small, formerly of Nashville, Tenn., has been appointed staff physician of the bureau of maternal and child health of the state board of health.

Changes in State Medical Board.—Dr. Robert E. Flynn, La Crosse, was appointed to the State Board of Medical Examiners by Governor Heil September 13. He succeeds Dr. Cornelius H. Cremer, Cashton. At a recent meeting in Milwaukee Dr. George R. Reay, La Crosse, was elected president of the board and E. C. Murphy, D.O., Eau Claire, was elected secretary.

Society News.—Drs. Ethel C. Dunham of the Children's Bureau, Washington, D. C., and Wyman C. C. Cole, Detroit, addressed the Milwaukee Pediatric Society October 11 on "Organization of the Pediatric and Obstetric Groups in a Campaign to Reduce Neonatal Mortality" and "Cyanosis of the Newborn" respectively.——Dr. Jay Arthur Myers, Minneapolis, addressed the Medical Society of Milwaukee County, Milwaukee, October 13 on "Controlling Tuberculosis in a Community." The meeting was a memorial to the late Dr. Hoyt E. Dearholt, for many years secretary of the Wisconsin Antituberculosis Association. Dr. Gilbert E. Seaman, Winnebago, gave an address on Dr. Dearholt's contributions to medicine and tuberculosis.

PHILIPPINE ISLANDS

University News.—Dr. Antonio G. Sison, dean of the College of Medicine, University of the Philippines, Manila, has been appointed director of the Philippine General Hospital also. The work of the hospital will be coordinated with that of the various units of the medical school, according to the *Journal of the Philippine Islands Medical Association*. President Quezon also authorized the establishment of a graduate school in the medical college in accordance with provisions of a law appropriating money for the purpose.

GENERAL

Ophthalmic Board to Hold One Written Examination.—The American Board of Ophthalmology announces that only one written examination will be held in 1940. This will be in various cities throughout the country March 2. All applications for this examination must be received before January 1 and all applicants must pass a satisfactory written examination before being admitted to the oral examination. Candidates planning to take the next oral examination, which will be in New York June 8-10, 1940, must file their case reports before March 1. The date of the fall examination will be announced later. For application blanks write at once to the secretary of the board, Dr. John Green, 6830 Waterman Avenue, St. Louis.

Medical Fellowships Available.—Fellowships in the medical sciences administered by the medical fellowship board of the National Research Council will be available for the year beginning July 1, 1940. These fellowships are open to citizens of the United States or Canada who have a Ph.D. or an M.D. degree and are intended for recent graduates rather than for persons already established professionally. The fellows will be appointed at a meeting to be held about March 1 and applications must be filed on or before January 1. For further information address the Secretary, Medical Fellowship Board, National Research Council, 2101 Constitution Avenue, Washington, D. C. Dr. Alfred Blalock, Nashville, Tenn., and Homer W. Smith, D.Sc., New York, have been appointed members of the board.

Ohio Valley Allergists' Meeting.—The Ohio Valley Allergy Society held a meeting in Cincinnati October 28-29. Following a general discussion of "Potassium Chloride Therapy in Allergic Diseases," the speakers were:

Dr. Jonathan Forman, Columbus, Histaminase Therapy in Allergic Diseases.
Dr. John H. Mitchell, Columbus, Emphysema—The Importance of the Excursions of the Diaphragm in Estimating Prognosis—Breathing Exercises.
Dr. George E. Rockwell, Cincinnati, Present Status of Tetanus Toxoid—Advisability of Its Use in Immunizing Horse Serum Sensitive Individuals.
Dr. Armand E. Cohen, Louisville, Ky., The Asthma Syndrome Due to Heart Disease.
Dr. Caryle B. Bohner, Indianapolis, Aspirin-Sensitive Asthmatics.

Special Society Elections.—Dr. Waller S. Leathers, Nashville, Tenn., was chosen president-elect of the American Public Health Association at the annual meeting in Pittsburgh October 16-20, and Dr. Edward S. Godfrey Jr., state health officer of New York, Albany, was installed as president. Vice presidents elected were Miss Elizabeth L. Smellie, R.N., chief superintendent of the Victorian Order of Nurses for Canada, Ottawa, Ont.; Dr. Domingo L. Ramos, Fabrica, P. I., and Dr. Wilton L. Halverson, Pasadena, Calif. The 1940 convention will be held in Detroit.——Dr. Evarts A. Graham, St. Louis, was chosen president-elect of the American College of Surgeons at its annual session in Philadelphia October 19. Drs. Oliver S. Waugh, Winnipeg, Man., and Albert O. Singleton, Galveston, Texas, were elected vice presidents and Dr. George P. Müller, Philadelphia, was installed as president.

European Journals and the War.—The American Documentation Institute requests that subscribers to European chemical or other scientific journals who do not receive their copies report the matter promptly. The cultural relations committee of the institute hopes to be able to surmount such war obstacles as interrupted transportation, embargoes and censorship, which seriously affected the progress of research during the last war. It is hoped that the principle will be established that materials of research having no relation to war shall continue to pass freely, regardless of the countries of origin or destination. Reports with full details of where subscription was placed and name and address of subscriber, volume, date and number of the last issue received should be addressed to the American Documentation Institute, Bibliofilm Service, U. S. Department of Agriculture Library, Washington, D. C.

Southwestern Medical Association.—The twenty-fifth anniversary postgraduate conference of the Southwestern Medical Association will be held at the Hotel Cortez, El Paso, Texas, November 9-11. The program will consist of general assemblies, clinical and pathologic conferences, motion picture demonstrations and round table luncheons. The speakers will be:

Dr. Fred H. Albee, New York, orthopedic surgery.
Dr. Marye Y. Dabney, Birmingham, gynecology.
Dr. Leo Eloesser, San Francisco, surgery.
Dr. Samuel D. Ingham, Los Angeles, neurology.
Dr. Julius Lempert, New York, otology.
Dr. Charles F. McCuskey, Glendale, Calif., anesthesia.
Dr. Louis H. Newburgh, Ann Arbor, Mich., dietetics.
Dr. Henry M. Winans, Dallas, Texas, medicine.

A special feature of the meeting will be the presentation of a "Medical March of Time" by charter members of the association.

Dana Medal Awarded to Dr. Ellett.—The Leslie Dana Medal, awarded annually by the St. Louis Society for the Blind for "outstanding achievements in the prevention of blindness and the conservation of vision," was presented to Dr. Edward C. Ellett, Memphis, Tenn., at a dinner in St. Louis October 14. The presentation was to be made by Dr. Edward Jackson, Denver, first recipient of the medal in 1925, and another speaker was Mr. Lewis H. Carris, New York, general director of the National Society for the Prevention of Blindness, which cooperates in the selection of the recipient. Dr. Ellett, who is 69 years old, has practiced ophthalmology in Memphis since 1893 and was professor of diseases of the eye at the University of Tennessee College of Medicine from 1906 to 1922. He is a former president of the American Academy of Ophthalmology and Otolaryngology and of the American Ophthalmological Society and chairman of the Section on Ophthalmology of the American Medical Association.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Oct. 7, 1939.

A Healthier Nation

It is interesting that the annual report of the Ministry of Health, which of course was compiled before the outbreak of the war, shows that as we enter a period of destruction the health of the nation was never so good. The average weight of school children at the age of 12 has increased by 3 pounds and the average height by half an inch compared with ten years ago. The same tendency was shown in the medical examination of the conscripts, of whom nearly 83 per cent passed as grade 1. The death rate has again fallen and is now 8.5 per thousand of population, the lowest on record, just half what it was in 1901. Infant mortality has a new low record of 53 per thousand births, little more than one third of what it was at the beginning of the century. Maternal mortality in 1938 was less than 3 per thousand births, while only five years ago it was 4.4. The deaths from tuberculosis were again the lowest on record, being only half the number in 1911. But there has been a rise in the cancer mortality, the deaths numbering 68,605, which was 1,600 more than in the previous year.

Great progress has been made in the control of infectious diseases. Environmental diseases, such as cholera, typhus and plague, have almost entirely disappeared and the cases of typhoid have been substantially reduced. But the position is not so satisfactory with regard to diphtheria, of which the number of cases fluctuates from year to year without showing any general decline. There are about 3,000 deaths from typhoid every year. There has been no material decrease in the incidence of influenza, measles and whooping cough, but the death rate from these diseases has considerably declined. Comparison of the deaths per million of population for 1938 with the average for the decade 1921-1930 shows influenza 118 against 369, measles forty against 109, whooping cough twenty-seven against 114. In 1938 only eighteen cases of smallpox were notified, from which there were three deaths, the first since 1934. An exceptionally large number of cases of poliomyelitis, 1,489, were notified, almost twice those of the previous year.

Women Physicians in the Army

Following representations by the British Medical Association, a scheme has been authorized for the employment of women physicians with the army medical services in the war. They will be eligible for employment either as civilian medical practitioners or medical officers attached to the army medical corps with a military status. Civilian medical practitioners will be engaged under the same conditions and rates of remuneration as male practitioners. For the army medical corps they will first be accepted as medical officers with the relative rank of lieutenant but without a commission. They will receive advancement in relative rank as for the medical corps in war. They will wear a uniform to be decided on and will receive the same pay and allowances as for officers of the corps, except that their rations will be four fifths of those given to males (the accepted principle of all women personnel in the army).

Ambulance Trains Under Construction

The British railways are engaged in the construction of a number of ambulance trains for use both at home and oversea. Work has already been completed on several trains and, to enable more to be brought into service rapidly, work on different sections has been entrusted to seven railway workshops throughout the country. Each train is fully equipped with cars for traveling staffs of nurses, physicians, kitchens and wards. Casualty evacuation trains have also been built for use in the event of air raids, in order to assist in the distribution of injured civilians throughout the country. The fitting up of the trains includes electric lighting and steam heating and many devices to ensure the comfort of patients.

The Danger of Traction on the Scalp in Placenta Praevia

In 1925 J. A. Willett introduced a method of treating placenta praevia by traction on the fetal scalp with a forceps which he devised. This was applied to the scalp with a wide bite and traction was made by attaching a weight not exceeding 2 pounds. In Great Britain Willett's forceps has been extensively used. At the Section of Obstetrics and Gynecology of the Royal Society of Medicine, Prof. F. J. Browne stated that in a series of 3,103 cases of placenta praevia which he had collected and analyzed from the reports of eleven teaching hospitals it was used in 252 with a maternal mortality of 3.5 per cent and a fetal mortality of 46.4 per cent. The advantages claimed for the forceps are that (1) it can be applied when the os admits only one finger and therefore is too small to allow a foot to be brought down; (2) little internal manipulation is necessary; (3) the fetus is spared the dangers of breach delivery and the fetal mortality is therefore lower than after version. The average fetal mortality under all methods of treatment in this series was 54.2 per cent, so that there seems some justification for the last claim. But Browne has recently had two cases in which the use of the forceps was followed by Bacillus welchii infection of mother and fetus.

In the first case a secundipara aged 32 was admitted after losing about half a cupful of blood. She was thirty-two weeks pregnant. The position was left occipito-anterior high above the pelvic brim. A tentative diagnosis of placenta praevia was made and she was treated expectantly, but bleeding recurred three and eight days later and she was examined under anesthesia. The cervix admitted one finger and the placenta was felt to extend to the internal os. The membranes were ruptured and Willett's forceps was applied with a weight of 1½ pounds attached. Two days later labor pains had not begun, the temperature was 102 F. and there was a foul smelling discharge but no further bleeding. Pains began next day, when the temperature was 103 and the pulse 150. A dead fetus was born. It and the placenta were putrid. The mother's condition was so bad that a transfusion was done and B. welchii serum was given. Next day crepitations were felt in the abdominal wall and she died on the following morning. The necropsy showed gas bubbles in the rectus muscle and the blood vessels.

The second patient was a primigravida aged 28, admitted for bleeding of one week's duration. She was eight days overdue and the vertex was not engaged. She was treated expectantly, but as slight bleeding continued she was examined under anesthesia after nine days. The os admitted one finger with difficulty and the edge of the placenta was felt 1½ inches above the internal os. The membranes were ruptured and Willett's forceps was applied. Weak pains began and after nine hours the forceps came off spontaneously. Labor progressed slowly and after four days a putrid fetus was born. B. welchii serum was given intramuscularly as a prophylactic. The mother recovered. Cultures from the cervix showed B. welchii, numerous colon bacilli and a few fecal streptococci. Cultures from the fetal spleen grew B. welchii.

Browne pointed out that in applying Willett's forceps a more or less lacerated wound of the fetal scalp is necessarily made. The weight enables the fetal head to compress the placenta, but this compression arrests both the maternal and the fetal

circulation of the placenta, which is liable to kill the fetus and produces ideal conditions for infection by the Welch bacillus—a ragged wound in dead tissues. If the bacillus is present in the vagina or gains access to it, infection and gas gangrene are likely. It has been shown by Hill, of Melbourne, that this bacillus is widely distributed. He found it in the floor dust of labor wards and on the hands of medical attendants after washing and drying. Browne concluded that Willett's forceps should have no place in the treatment of placenta praevia.

PARIS

(From Our Regular Correspondent)

Sept. 27, 1939.

Polypeptides in General Medicine and Psychiatry

Laignel-Lavastine revived the history of polypeptides before the Academy of Medicine by investigating the comparative value of polypeptidemia in blood urea, both in general practice and in psychiatry. Between 1928 and 1934 polypeptides were an object of infatuation among investigators, who now are somewhat disappointed, perhaps because they expected too much. According to Laignel-Lavastine and his collaborator Duguet, loss of interest in polypeptides is hardly reasonable. The sequence of chemical disintegrations which carries albumin to the urea includes polypeptides, intermediate between peptones and the amino acids. The chemical entity of these polypeptides is far from being precisely known. Polypeptides are defined by their precipitations induced by means of trichloroacetate and phosphotungstic acid, and their quite delicate dosage is based on these reactions. Goiffon and Spacey proposed a simpler and precise, though indirect, method, namely measuring the tyrosine content of the blood polypeptides. This is, in fact, quite regular in polypeptides though Fischer obtained some synthetically which did not contain any.

Pierre Duval draws from the dosage with polypeptides prognostications of interest to surgeons, namely that in those with extensive burns and in numerous cancer patients polypeptidemia is elevated.

In general medicine, Fiessinger has shown that hypopolypeptidemia, or at least an increased deamination index, is always high in hepatic insufficiency. A study of sixty cases (forty from the general practice, twenty from psychiatry) indicated to Laignel-Lavastine the same increase of the rate of polypeptidemia in hepatic cases but accompanied with a low azotemia rate. In mental cases, however, the polypeptidemia and azotemia rate is higher than the normal rate. This hyperpolypeptidemia is especially noticeable in senile dementia, confusion amentia, mania and alcoholism; diseases of patients of this class as a rule are accompanied with hepatic insufficiency. Whenever hyperpolypeptidemia is marked (tyrosine index of more than 100 mg.), prognosis is grave. On the other hand, polypeptidemia can shed light on the nature of certain pronounced azotemias (2 Gm. or more). If the polypeptidemia rate is moderately high, azotemia is often transitory and indicates merely renal lesions in their final stage. Claude likewise studied the variations of the polypeptide rate in the cerebrospinal fluid in the course of dementia paralytica and other mental conditions. Generally in catatonia not due to lesions the polypeptidemia rate is variable and does not suggest parallelism with the condition of the liver. In alcoholic psychosis it varies according to the organic condition of the patients. Normal in chronic alcoholic patients, it as well as the deamination index increases in acute or subacute cases. In dementia paralytica the polypeptides of the spinal fluid are probably increased by a disorder of nitrogen metabolism in consequence of brain modifications. No valid diagnostic or prognostic indications can be deduced from these investigations, at least in the field of mental diseases.

Cancerigenic Effect of Leprous Tissue

Professor Peyron, in collaboration with Sister Marie Suzanne, an investigator of leprosy, took from a leper of the mixed type (N^1 L^2) portions of a leproma of the jaw and kept it for fifty days in distilled water, where it underwent little change. On the fiftieth day a large quantity of Hansen's bacilli were found giving clear histologic proof of the leprous nature of the tumor. These leprous portions were mixed with an emulsion and injected into the scrotum of four adult rats and into the axillary and inguinal regions of three adult female rats. The female rats manifested no other reaction outside the common reabsorption granuloma. Two of the male rats developed a perceptible tumor in the third month. The first rat had an enormous scrotal tumor encroaching on the abdomen and a pleural metastatic swelling 2.5 cm. in length. The tumor presented all the traits of malignant tumors of the interstitial cells together with significant indications of dedifferentiation, in keeping with its malignant nature manifested by general signs of carcinomatous intoxication. In the second rat, killed before the other, the tumor was still benign but histologically all the more characteristic. No doubt can exist on the causal relation between the injection of leprous tissue and the appearance of the tumors. Spontaneous tumors in the interstitial glands of the testicles are rare. In the large collection of the Croker Institute and among the large number of rat tumors none have been found. Hence Peyron's leprous tissue products are of great interest. They could have been caused only by the bacillus itself or the products of the autolysis of the leproma. Neither of these hypotheses can be considered satisfactory in our present state of knowledge of experimental carcinoma. Nevertheless one can invoke in favor of the former assumption observations of Jensen's sarcoma, the appearance of which was likewise provoked by the injection of acid-resisting bacilli derived from a pseudotuberculosis of the intestine of an ox.

Radiotherapy in Uterocervical Carcinomas

It seems that uterocervical carcinomas are slightly on the increase. At any rate they occupy an important place in the deaths from cancer. Last June at the meeting of the Société de gynécologie obstétrique de Paris Dr. Simone Lacore Laborde set forth the results obtained by radiotherapy in cervical cancers at the Cancer Institute of the Faculty of Medicine of Paris. The classification adopted by the speaker is that of the subcommittee on cancer of the League of Nations and is divided into four stages. In the first stage, lesions are strictly confined to the cervix. In the second stage the parametrium is infiltrated. This stage includes the cancers at the upper part of the vagina. In the third stage, cancerous growth has reached the pelvic region or, rather, the vagina as far as the lower area. Isolated metastases may also be noted. In the fourth stage the cancer infiltration extends more or less to the neighboring organs, the bladder or rectum or it spreads to a greater distance. In the ten years from 1921 to 1932, 813 cervical carcinomas in the four stages were observed at the Institute of Cancer and 592 were treated: forty in the first stage, ninety-two in the second, 284 in the third and 176 in the fourth. Of the 592 patients, 384 were alive and without recidivation at the end of five years, 384 had died in the course of the five years and six had had a recurrence. One hundred and sixty-seven were living and without recidivation after five years. The proportion of cures during the five years varied according to the years between 12 and 37.9 per cent, the average being 28.2 per cent. There was the same difference according to the stages: fifty-seven, or 5 per cent, in the first stage; forty-eight, or 9 per cent, in the second; thirty-one, or 6 per cent, in the third, and only five in the fourth. The therapy employed was based on the combined use of radium and roentgen rays. Radium therapy was performed by means of tubes containing 10 mg. of radium with a filtration equiva-

lent to 1 mm. of platinum. For the roentgen therapy, high voltage was used with a 300, 400 and even 500 kilovolt pressure. Massive irradiation was refrained from because it induced a general shock without yielding better results. Teleradium therapy by means of an apparatus containing 5 Gm. of radium and permitting irradiations at 20 cm. from the level of the skin did not prove superior to classic methods. Technics of irradiation seem to commend themselves in preference to excision. According to Heyman (1927), surgery's record for cures is only 18 per cent on the average. Besides, one must consider the operative risks (from 7 to 9 per cent), whereas the mortality due to roentgen rays does not exceed 3 per cent.

BERLIN

(From Our Regular Correspondent)

Sept. 10, 1939.

The Abuse of Hypnotics

The public health department of the reich has just published information regarding the use of sleep inducing drugs. It has instituted an inquiry in about 250 clinics, hospitals and centers for mental diseases to secure exhaustive data of the extent of the use of these drugs. It plans to propose that all such drugs as well as pain allaying preparations containing barbituric acid derivatives be dispensed only on medical certification. The greatest attention has officially been given to this ever present problem and the impression may have been created that the use of these drugs has declined. However, the information given to the public health department by relatives of sleeping drug addicts, by physicians, by druggists, by medical district associations, by the police, by health bureaus and by administrative authorities has been so copious that the conclusion is inevitable that the use of these drugs is on the increase. Observations have been made that opium addicts, in consequence of the enforcement of antinarcotic measures, now resort to hypnotics, which they can easily obtain since a medical prescription is not necessary. It is also said that the combined action of alcohol and barbituric acid is mutually intensifying. The public health department has information indicating that hypnotics not requiring prescriptions are increasingly ordered in large quantities by individual users. The use of hypnotics also gives rise to a diagnostic problem. Professor Bonhoeffer, psychiatrist in Berlin, reported that within the last decade wrong diagnoses, previously unknown, of brain tumors had become more numerous, owing to the fact that persons with chronic barbituric acid intoxication had concealed the use. He mentioned among deceptive symptoms slowly increasing stupor, speech disturbances, nystagmus and loss of abdominal reflexes. Professor Pohlisch, psychiatrist in Bonn, reported the case of a university professor who was dismissed because of alleged hereditary epilepsy and for whom sterilization was recommended. It was then discovered that the chronic use of hypnotics was the cause of his condition.

Efforts to Use Workers Who Are Chronically Ill

In view of the great demand for workers in Germany it is especially important to examine the possibilities of economic adjustment for those with chronic ailments. Two series of lectures of a postgraduate nature were recently given at the Berlin Academy for Physicians, on the significance of primary symptoms for timely therapy and prophylaxis, especially with reference to workers, and on economic adaptation of workers with chronic ailments. The lectures were intended to supply information to factory physicians and assistant physicians in charge of departments and practicing physicians interested in these questions. Explanations by state secretary Syrup of the economic needs in the four year plan formed the basis of all the lectures. In Germany, not counting Bohemia and Moravia, 40,000,000 persons are employed in industry. In 1936 lack of skilled laborers became noticeable. Reserves of male workers are no longer available. Replacement of men with women brings with it dangers to their health. It is essential for public welfare that workers be adjusted to the jobs by which they can maintain themselves. Responsibility for this rests largely on physicians, especially factory physicians. The factory physician should inform himself on how workers live, their family conditions and so on, all of which are important factors affecting efficiency. Treatment of sick workers is not his function; however, he may represent the patient's physician in supervising directions given by him. Observations of slight, scarcely measurable pathologic changes, of scarcely noticeable decrease in efficiency and of early recognition of harmful symptoms might constitute valuable information for the maintenance of health of workers. By observing health measures in a factory and the habits of individual workers the factory physician may, like a seismograph, observe every change in the frequency of diseases and accidents and obviate or relieve them by determining the causative factors. He will have to work in close cooperation with the management. Observations of large groups at work and the evaluation of extensive observational data representing an accumulation of more than 350,000 cases may open up a new field of medical territory. The scarcity of qualified labor has made necessary the employment of those physically below par and involves increased obligations for the cooperating and supervising factory physicians.

ECONOMIC EMPLOYMENT

The second series of lectures, on the economic employment of persons with chronic ailments, was supplementary to the first. The care of such persons constitutes a heavy drain on social insurance reserves. To what extent persons with chronic ailments are dependent on social insurance has not been determined statistically. However, the statistics furnished by individual sick funds and state insurance companies in the provinces offer some information. Among those chronically ill are persons with tuberculosis, cancer, cardiac and vasomotor diseases, diabetes, and those with gastric and intestinal disturbances. It is of little value for such persons to be declared by the physician in charge as fit or unfit for work. At present fitness for work is determined by the social insurance physicians, who work in close cooperation with the public health office, the labor department and the practicing physician in the detection of public diseases. The practical operation of such cooperative services is discernible, for example, in the clinic established in Berlin to determine diabetes. At present, 14,300 diabetic persons, including 118 married couples, are served there.

CARE OF EMPLOYEES

Through arrangements, workers who are not entirely unfit physically can do satisfactory work connected with the soil or excavation. Factory workers with circulatory disorders in charge of machines with rotating belts can easily receive injury, though the work is not difficult. The factory physician should be consulted in determining the speed with which work of this kind should be done. Rational arrangement may enable the injured and even persons with amputated limbs to work. In the case of women, often it is not the heavy work, but certain harmful effects like constant vibrations and injuries caused by continued foot manipulations that are significant. These explanations, elaborated by detailed discussions in lectures, show how effort is made to utilize the working ability of every one by exhausting all possible medical knowledge.

Water Requirements of Workers Under Heat Pressure

Dr. Hebestreit expressed himself in the new periodical *Health Guidance of the German People* on the water requirements of workers under heat pressure. Workers who toil under conditions of great heat lose on an average more than a gallon of water during a working day of eight hours. This loss should

be compensated by drinking during work. However, every excess is to be avoided in order not to burden the circulation and to prevent gastric troubles. Above all, beverages taken should not be too hot or too cold, but lukewarm or of the temperature of the room. Beer and mineral waters are not suitable. Coffee should be drunk with the addition of milk. In the stoker rooms of ships, gruel made for example of oats and rice has proved its worth. It slakes the thirst well and supplies the body with salts to replace those lost in perspiration. For that reason gruel is to be recommended to workers under similar heat conditions. In place of black tea, which has no appetizing taste at room temperature, teas of native growth are recommended, such as teas made from blackberry and strawberry leaves or from peppermint. To supply the body with easily absorbable food values during great physical exertion, sugar can be added to the tea; to supplement loss of salts, from 2 to 3 Gm. of salt per quart of beverage can be added without noticeably impairing its taste.

Marriages

PETER A. N. PASTORE, Bluefield, W. Va., to Miss Julia Anna Rourke of Prides Crossing, Mass., at Rochester, Minn., September 14.

CHARLES WESTON WARREN, Upperville, Va., to Miss Geraldine Estelle Mitchell of Winston Salem, N. C., recently.

WILLIAM GREGORY THALMANN JR., Philadelphia, to Miss Sara Carpenter Klopp of Rosemont, Pa., September 30.

FERDINAND E. CHATARD IV, Baltimore, to Miss Constance Bentley Lyon of Purcellville, Va., September 9.

NEEDHAM BRYANT BATEMAN to Miss Florence Estele Stevenson, both of Atlanta, Ga., September 4.

JAMES A. BRADLEY to Mrs. Evelyn Neuling, both of St. Petersburg, Fla., in Tampa, October 1.

FRANKLIN LEROY WILSON, Montreat, N. C., to Miss Eleanor D. Garrett of Miami, Fla., September 7.

ROBERT LEE SANDERS, Columbia, S. C., to Miss Helen Jessa McDowell of Charleston, September 23.

CHARLES E. CONNER, Wenatchee, Wash., to Miss Marthe Irwin of Colorado Springs, July 15.

JOSIAH HARRIS SMITH, Selma, Ala., to Mrs. Gladys Buckmaster Wire at Cincinnati in August.

PERCY F. GUY, Seattle, to DR. MAY A. BORQUIST of Honolulu, Hawaii, in Portland, July 15.

IRVING W. SALOWITZ, to Miss Dorcas Marie Crook, both of Plymouth, Ill., September 24.

JOE M. VANHAY, New York, to Miss Helen Spangler of Greenville, N. C., September 6.

LEON BLUM, Far Rockaway, N. Y., to Miss Janette Goldstein of Atlanta, Ga., August 8.

J. ELLIOTT ROYER, Oakland, Calif., to Miss Helen Hay of Pasadena, Calif., September 28.

PAUL B. WILSON to Miss Esther Elizabeth Roberts, both of Philadelphia, September 25.

EARL STOUGH TAYLOR to Miss Virginia Hanson, both of New York, September 23.

SIDNEY F. YUGEND, Sigourney, Iowa, to Miss Bertine Hooper of Hartford, September 8.

HARRY D. TRIPP to Miss Elizabeth Kopp, both of Logansport, Ind., September 30.

FREDERICK R. MINNICH to Miss Katherine Calhoun, both of Atlanta, Ga., recently.

WALTER SHRINER, Elgin, Ill., to Miss Ruth Arline Shearer of Aurora, August 26.

WILLIAM S. COLE, Seattle, to Miss Catherine Rutledge of Burlington, August 5.

LEON E. POLLOCK to Miss Jean Berry, both of Spokane, Wash., August 13.

FRANCIS SAUER, Canton, Ohio, to Miss Irma Dotts at Carrollton, August 14.

JOHN B. DYNES to Miss Edna Bradbury, both of Boston, September 22.

Deaths

William Bricker Chamberlin ✠ Cleveland; Western Reserve University Medical Department, Cleveland, 1900; secretary of the Section on Laryngology, Otology and Rhinology of the American Medical Association from 1918 to 1922 and chairman from 1922 to 1923; clinical professor of otolaryngology at his alma mater and at various times associate clinical professor, assistant clinical professor, associate and instructor in otolaryngology; member, past president and vice president of the American Laryngological Association; member, past president and secretary-treasurer of the American Bronchoscopic Society; past president of the Cleveland Association for the Hard of Hearing and of the Cleveland Academy of Medicine; member of the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; on the staff of the University Hospitals of Cleveland; aged 65; died, September 5, in Cleveland Heights of coronary sclerosis and thrombosis.

Arthur Godfrey Fort ✠ Atlanta, Ga.; Atlanta College of Physicians and Surgeons, 1904; past president of the Medical Association of Georgia; member of the American Academy of Ophthalmology and Otolaryngology and the Southeastern Surgical Congress; fellow of the American College of Surgeons; instructor of ophthalmology at the Emory University School of Medicine, 1918-1924; commissioner of health of Irwin and Tifton counties in 1916; served at various times and in various capacities on the staffs of the Piedmont Sanitarium, Wesley Memorial Hospital, Georgia Baptist Hospital, Crawford W. Long Memorial Hospital and the Grady Hospital; aged 61; died, September 15, in the Emory Hospital of myocarditis and pulmonary edema.

Albert Bernard Yudelson ✠ Chicago; Northwestern University Medical School, Chicago, 1906; associate professor of medical jurisprudence and nervous and mental diseases at his alma mater; member of the Central Neuropsychiatric Association; past president of the Chicago Neurological Society; served during the World War; attending neurologist to the Cook County Hospital and the Wesley Hospital; aged 67; died, August 27, of coronary thrombosis.

John William McIntosh, Burnaby, B. C., Canada; University of Toronto Faculty of Medicine, 1894; formerly medical officer of health of Burnaby and Vancouver; served during the World War with the Canadian Army; from 1916 to 1920, was a member of the provincial legislature; past president of the Canadian Public Health Association; aged 68; died, August 12.

William Garretson Carhart, Fort Lyon, Colo.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; served during the World War; instructor of pathology and bacteriology at the University of Missouri, Columbia, from 1904 to 1907; on the staff of the Veterans Administration; aged 65; died, September 17, of coronary occlusion.

Bennett Sheldon Beach ✠ New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1887; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; on the staff of the New York Eye and Ear Infirmary; aged 77; died, September 13.

Thomas Edward Parker, Waterbury, Conn.; Yale University School of Medicine, New Haven, 1904; member of the Connecticut State Medical Society; served during the World War; on the staff of St. Mary's Hospital; aged 58; died, August 1, in the New Haven (Conn.) General Hospital of diabetes mellitus and pyelitis.

William A. Zellars, Shaker Heights, Ohio; College of Physicians and Surgeons, Baltimore, 1891; formerly president of the board of education of Freeport, postmaster and member of the county board of education; at one time president of the bank of Freeport; aged 73; died, August 11, in Cleveland of uremia.

David Ernst Matzke, Punxsutawney, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1925; member of the Medical Society of the State of Pennsylvania; served during the World War; on the staff of the Punxsutawney Hospital; aged 40; died in August of acute dilatation of the heart.

Roy George Pfotzer ✠ Buffalo; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1924; associate in medicine, University of Buffalo School of Medicine; fellow of the American College of Physicians; on the staff of the Millard Fillmore Hospital; aged 46; was drowned, August 9.

Cooper Curtice, Beltsville, Md.; Columbian University Medical Department, Washington, D. C., 1888; formerly associated with the Bureau of Animal Industry, U. S. Department of Agriculture; was known for his researches on cattle tick fever; aged 83; died, August 8, of coronary occlusion.

Charles W. Bankes, Middleport, Pa.; College of Physicians and Surgeons, Baltimore, 1881; member of the Medical Society of the State of Pennsylvania; bank president; aged 82; on the associate staff of the Pottsville (Pa.) Hospital, where he died, August 27, of cerebral hemorrhage.

Paul Whiting Woodruff ✠ Chatfield, Minn.; State University of Iowa College of Medicine, Iowa City, 1933; formerly resident to the Chicago Lying-in Hospital and Dispensary; aged 34; died, August 16, in a hospital at Winona, Miss., of injuries received in an automobile accident.

John Joseph Shea, San Diego, Calif.; Harvard Medical School, Boston, 1897; member of the California Medical Association; at one time member of the board of health of Beverly, Mass.; aged 70; died, August 19, in the Mercy Hospital of hypertrophy of the prostate and uremia.

Charles A. Duffy ✠ Pittsburgh; Georgetown University School of Medicine, Washington, D. C., 1910; fellow of the American College of Surgeons; on the staff of the Southside Hospital; aged 52; died, August 26, in the Buffalo (N. Y.) General Hospital of coronary occlusion.

Walter Algeno Allen ✠ Hampstead, N. H.; Dartmouth Medical School, Hanover, 1893; served during the World War; for many years member of the school board and board of health; formerly state senator; aged 70; died, August 23, in the Benson Hospital, Haverhill, Mass.

Leone Franklin La Pierre, Norwich, Conn.; Yale University School of Medicine, New Haven, 1901; member of the Connecticut State Medical Society; for many years on the staff of the William W. Backus Hospital; aged 62; died, August 7, of cerebral hemorrhage.

Hiram Bachelder West, Los Angeles; Dartmouth Medical School, Hanover, N. H., 1900; member of the American Psychiatric Association; on the staff of the Veterans Administration Facility, West Los Angeles; aged 59; died, August 11, of coronary thrombosis.

Edgar Jonas Knapp, Rice Lake, Wis.; Harvard Medical School, Boston, 1892; member of the State Medical Society of Wisconsin; aged 72; died, August 29, in the Veterans Administration Facility, Fort Snelling, Minn., of carcinoma of the duodenum.

John Ludwig Loutfian, Coxsackie, N. Y.; Medico-Chirurgical College of Philadelphia, 1902; member of the Medical Society of the State of New York; village health officer; aged 64; died, August 5, in the Albany (N. Y.) City Hospital.

Caroline Le Monte Rolph Bassmann, Claremore, Okla.; Northwestern University Woman's Medical School, Chicago, 1897; member of the Oklahoma State Medical Association; aged 70; died, September 30, in St. John's Hospital, Tulsa.

Raymond Alexander Turnbull, Elmira, N. Y.; University of Buffalo School of Medicine, 1904; member of the Medical Society of the State of New York; served during the World War; aged 58; died, August 13, in St. Joseph's Hospital.

Edwin C. Bandy, Alabama City, Ala.; Medical College Montezuma University, Bessemer, 1898; member of the Medical Association of the State of Alabama; aged 78; died in September in Gadsden of extensive burns and bronchopneumonia.

Oliver Hines Finnical, Cadiz, Ohio.; Starling Medical College, Columbus, 1895; member of the Ohio State Medical Association; aged 67; died, September 9, in the Ohio Valley General Hospital, Wheeling, of cerebral thrombosis.

Franklin J. Cushman ✠ Lansing, Mich.; Detroit College of Medicine and Surgery, 1921; member of the American Urological Association; served during the World War; aged 42; died, September 11, of bilateral renal calculus.

James Merlin Fitzgerald ✠ Chicago; Jenner Medical College, Chicago, 1908; professor of mental physiology at Bennett Medical College, 1903-1910; aged 69; died, August 16, in San Francisco of carcinoma of the bladder and liver.

Harper Leonidas Crow, Bossier, La.; University of Louisville (Ky.) Medical Department, 1913; served during the World War; aged 53; was killed, September 3, when the truck in which he was driving overturned.

Albert Earl Reed ✠ Larned, Kan.; Rush Medical College, Chicago, 1905; secretary of the Pawnee County Medical Society; medical director of the Larned City Hospital; aged 58; died, August 30, of coronary occlusion.

George T. Van Cleve, Malden, Mo.; University of Louisville (Ky.) Medical Department, 1879; member of the Missouri State Medical Association; aged 86; died, August 5, in the Baptist Hospital, Memphis, Tenn.

Fred Raines Morrow ✠ Fayetteville, Ark.; Memphis (Tenn.) Hospital Medical College, 1900; served during the World War; on the staff of the City Hospital; aged 68; died, August 15, of coronary embolism.

Frederick Ogle Roman, Washington, D. C.; National University Medical Department, Washington, 1894; member of the Medical Society of the District of Columbia; aged 73; died, August 12, of lymphatic leukemia.

Samuel T. Williams, Waynesburg, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1896; aged 70; died, August 4, in the Greene County Memorial Hospital of pulmonary edema following fracture of the femur.

Alfred Loomis Sawyer, Fort Fairfield, Maine; Medical School of Maine, Portland, 1907; member of the Maine Medical Association; served during the World War; aged 57; died, August 14, of acute pancreatitis.

Troy England Martin ✠ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1934; aged 29; on the staff of the Germantown Hospital, where he died, August 21, of streptococcic pneumonia.

James Edward Rudasill ✠ Markham, Va.; University of Pennsylvania Department of Medicine, Philadelphia, 1893; aged 67; died, August 2, in the Western State Hospital, Staunton, of hypertensive heart disease.

Elliott Benald Tobias, San Francisco; College of Physicians and Surgeons of San Francisco, 1921; member of the California Medical Association; aged 40; died, August 2, of coronary occlusion.

Paul Eskeberg, Miami, Fla.; Northwestern University Medical School, Chicago, 1938; member of the Florida Medical Association; aged 28; died, September 3, of chronic myelogenous leukemia.

Benjamin Franklin Hawk, West Palm Beach, Fla.; Columbus Medical College, 1891; aged 72; died, August 15, in the Veterans Administration Facility, Bay Pines, of carcinoma of the prostate.

Alfred Frederick Zittel, Buffalo; University of Buffalo School of Medicine, 1899; member of the Medical Society of the State of New York; aged 67; died, August 28, of carcinoma of the bladder.

Orville DeWitt Wescott, Walla Walla, Wash.; Rush Medical College, Chicago, 1904; on the staff of the Veterans Administration Facility; aged 68; died, August 29, of coronary thrombosis.

Paul Luttinger, New York; University and Bellevue Hospital Medical College, New York, 1911; member of the Medical Society of the State of New York; aged 54; died, August 11, of pneumonia.

George Lee Long, Fresno, Calif.; Hahnemann Medical College, San Francisco, 1886; formerly county health officer and county coroner; aged 81; died, August 12, of coronary occlusion.

John Henry Adams, Crockett, Calif.; College of Physicians and Surgeons of San Francisco, 1911; member of the California Medical Association; aged 51; died, August 16, in Oakland.

David Martin Levine, Detroit; Wayne University College of Medicine, Detroit, 1937; member of the Michigan State Medical Society; aged 28; died, August 7, of acute lymphatic leukemia.

Newton J. Boswell, Decatur, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1893; aged 66; died, September 8, of cerebral hemorrhage, arteriosclerosis and hypertension.

J. O. Bickham, Winchester, Ark.; Gate City Medical College, Dallas, Texas, 1903; aged 58; died, August 13, of myocarditis, acute dilatation of the heart, nephritis and hypertension.

Roy Lee Aiguier, Sulphur Springs, Texas; Southern Methodist University Medical Department, Dallas, 1914; served during the World War; aged 50; died, September 3, in Fort Worth.

James G. Robertson, Arrington, Tenn.; University of Tennessee Medical Department, Nashville, 1899; aged 77; died, August 21, in Cedar Hill, of carcinoma of the right side of the jaw.

Samuel A. Benson, St. Louis; Homeopathic Medical College of Missouri, St. Louis, 1896; aged 72; died, September 3, in the City Hospital of burns received when his home caught fire.

Thomas Jefferson Bouldin ⊕ St. Johns, Ariz.; Atlanta College of Physicians and Surgeons, 1901; past president of the Apache County Medical Society; aged 61; died in September.

James Henry O'Connor, St. Helena, Calif.; Columbia University College of Physicians and Surgeons, New York, 1899; served during the World War; aged 66; died, August 1.

John Henry Witbeck, Cayuga, N. Y.; Bellevue Hospital Medical College, New York, 1888; for many years health officer; aged 74; died, August 2, of a ruptured gastric ulcer.

Nathaniel Massie McKitterick, Burlington, Iowa; Rush Medical College, Chicago, 1880; formerly member of the state board of health; aged 81; died, August 29, of angina pectoris.

Adelbert D. Bowen, West Lodi, Ohio; Toledo Medical College, 1885; aged 79; died, September 2, in the Mercy Hospital, Tiffin, following an operation for strangulated hernia.

Thad S. Up de Graff ⊕ Pasadena, Calif.; Jefferson Medical College of Philadelphia, 1883; aged 74; died, August 2, in the Collis P. and Howard Huntington Memorial Hospital.

Norbert Vincent Mullin, Weymouth, Mass.; University of Pennsylvania Department of Medicine, Philadelphia, 1903; aged 59; died, August 18, in the Weymouth Hospital.

Edward Plotkin, Nashville, Tenn.; College of Physicians and Surgeons, Memphis, 1909; aged 56; died, August 24, in the Nashville General Hospital of cerebral hemorrhage.

Frederick A. York, Navasota, Texas; University of Texas School of Medicine, Galveston, 1898; aged 65; died, August 22, in the Brazos Valley Sanitarium of paralytic ileus.

Robert Fred Zeiss ⊕ New York; University of Texas School of Medicine, Galveston, 1916; member of the American Urological Association; aged 46; died, August 8.

Randolph D. Black, Cedar Grove, W. Va.; University of Nashville (Tenn.) Medical Department, 1903; aged 62; died, September 2, of carcinoma of the lumbar spine.

George William Lawler, Waukesha, Wis.; Milwaukee Medical College, 1908; aged 65; died, August 22, in the Waukesha Municipal Hospital of pneumonia.

Charles H. Davies, Kansas City, Kan.; Jefferson Medical College of Philadelphia, 1877; aged 86; died, September 16, of pernicious anemia and hypostatic pneumonia.

Frank J. Campbell, San Diego, Calif.; Chicago Medical College, 1890; aged 77; died, August 24, in the Mercy Hospital of cerebral hemorrhage and arteriosclerosis.

John H. T. Earhart, Westminster, Md.; University of Maryland School of Medicine, Baltimore, 1888; aged 77; died, September 10, of coronary thrombosis.

Howard Leon Sumner ⊕ Asheville, N. C.; Jefferson Medical College of Philadelphia, 1926; county health officer; aged 37; died, August 16, of heart disease.

William Henry Bennett, Fitchburg, Mass.; New York Homeopathic Medical College and Hospital, 1889; aged 75; died, August 3, of arteriosclerosis.

Alice Grace Charlton Guequierre, Wayne, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1922; aged 45; died, August 6, of carcinoma.

Thomas Raymond Thorn, Los Angeles; University of Texas School of Medicine, Galveston, 1927; aged 35; was killed, August 13, in an airplane accident.

George B. Hunter, Syracuse, N. Y.; Baltimore University School of Medicine, 1897; aged 64; died, August 25, in the University Hospital of pneumonia.

James Frank Hufford, Elrama, Pa.; University of Pittsburgh School of Medicine, 1910; aged 58; died, August 26, of uremia and arteriosclerosis.

Smith L. Bates, Adrian, Mo.; Medical College of Ohio, Cincinnati, 1878; aged 87; died, August 24, in a hospital at Kansas City of pneumonia.

Frank Alonzo Dearborn, Nashua, N. H.; Missouri Medical College, St. Louis, 1884; aged 81; died, August 3, of arteriosclerosis and heart disease.

James Henry Burnett ⊕ Kopperl, Texas; Atlanta (Ga.) Medical College, 1895; aged 67; died, August 22, of hypertension, nephritis and uremia.

Bureau of Investigation

THREE POSTAL FRAUD ORDERS

Durio Cosmetic Company

A CONTINUATION OF THE C. A. WILLIAMS FRAUD IS DEBARRED FROM THE MAILS

In this department of THE JOURNAL for Feb. 11, 1939, there appeared a brief story about the closing of the mails to the C. A. Williams Company, of McKamie, Ark. The title was a trade name used by two Negroes, C. A. Williams, who was 70 years old and who founded the business in 1929, and Ples L. Lewis, who in 1936 acquired a controlling interest (93 per cent) from Williams.

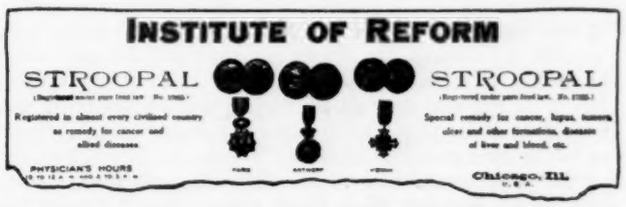
The concern sold a line of nostrums through the mails for the alleged cure of gonorrhea, syphilis, pellagra, paralysis, delayed menstruation, leukorrhea, rheumatism, "lung trouble," and so on. The Post Office authorities showed that the two men who conducted this swindle bought their preparations in gallon bottles from a St. Louis drug firm and then rebottled them into smaller bottles as needed. As the nostrums were quite worthless as cures for conditions for which they were sold, a fraud order was issued Aug. 23, 1938, closing the mails to the C. A. Williams Medicine Company.

But this did not stop the fraud. Williams and Lewis changed the name of their company and continued to do business at the old stand. The "C. A. Williams Company" became "Durio Cosmetic Company" and the sale through the United States mails of worthless swindles for the alleged cure of such diseases as syphilis, gonorrhea and pellagra went on. As a result the Post Office Department on March 3, 1939, issued a supplemental fraud order closing the mails to the Durio Cosmetic Company.

The Stroopal Fraud

A FAKE CANCER "CURE" BOBS UP AGAIN

The Stroopal case presents another example of how some slippery individuals attempt to evade fraud orders debarring them from the use of the United States mails. As long ago as 1930 the Post Office Department declared the Stroopal business of Chicago to be a fraud and closed the mails to this concern. The principal, Alphonse P. Faupel, however, continued



his business in the United States by operating it from London, England. The Post Office authorities, therefore, have found it necessary to issue a supplementary fraud order covering the London address.

The Stroopal cancer cure fraud originated in Germany many years ago with a self-styled "Professor" Stroop. It consists of three powders to be taken at monthly intervals when the moon is new! To the city bred this in itself might appear to arouse suspicion. But there are many otherwise intelligent country people who are still convinced that a calf should be weaned and the potatoes planted at certain phases of the moon. The advertising of Stroopal was declared *verboten* in Germany some years ago and so the headquarters of the fraud were transferred to London, where a greater degree of *laissez faire* was permitted. A Chicago branch was opened and for nearly twenty years the American branch of the fraud was conducted

from that city with agencies in Centralia, Okla., and Seneca, Kan. Most of the American business was directed to Americans of German descent, for much of the advertising was printed in German script.

According to Gehe's Codex (January 1913) Stroopal was nothing more marvelous than the powdered leaves of water germander or wood garlic (Teucrium scordium). In August 1930 the Post Office Department issued a fraud order barring Stroopal from the United States mails. The department brought out at the time that in the exploitation of Stroopal medals and "certificates of merit" were featured in the advertising and the claim was made that the product had been awarded these medals and certificates at exhibitions at Antwerp, Brussels and Paris. They were all utter fakes! It was shown, too, that when the importation of Stroopal was barred as dangerous to the health of the people the stuff was for a while smuggled into this country as "metal cleaning powder."

The scheme, and the government's action against it, were dealt with in an article in this department of THE JOURNAL for Oct. 4, 1930, and the matter in a condensed form appears in the book "Nostrums and Quackery and Pseudo-Medicine," volume III, published by the American Medical Association. Now, in 1939, the fraud again engages the attention of the United States Post Office Department. The Faupel quack was still selling his stuff to such victims as he could get in the United States from his office in London, England. As a result the fraud order issued in 1930 was supplemented by another issued March 6, 1939, closing the United States mails to the Stroopal Company and to Alphonse P. Faupel, both of London. All postmasters authorized to dispatch letter mail to England have been notified to return all letters addressed to the Stroopal concern to the senders with the word "Fraudulent" stamped plainly on the envelop. Also postmasters are warned not to issue any postal money orders payable to the Stroopal concern.

A Maté Fakery

PEREZ-MATÉ COMPANY OF BROOKLYN DEBARRED FROM THE MAILS

During the past few years attempts have been made to popularize in this country the South American beverage maté, also known as Paraguay tea. Yerba maté, while having a different flavor from that of the ordinary India or China teas of commerce, has the same physiologic effect. Like common tea it contains variable amounts of caffeine and tannin. To the average American palate maté seems to have a medicine-like taste and therefore it is not surprising that some of the promoters, finding it a poor seller as a beverage, endowed it with "patent medicine" qualities. As a pepper-up for weak men and frigid women it was apparently more of an economic success.

From Brooklyn one Arthur Koppel, using the trade style Perez-Maté Company, for about eight years put out maté under the names "Ola Maté," "Brazilian Maté" and "Para-Brazilian Maté." It was sold through the mails and the fraud order arm of the Post Office Department finally got around to it. According to the memorandum that Judge Vincent M. Miles, Solicitor for that department, sent to the Postmaster General, recommending the issuance of a fraud order, Koppel bought his Paraguay tea in bulk at 10½ cents a pound, repacked it and sold it for $2 a pound. According to Koppel's advertising, said Solicitor Miles, all users of his brand of maté would "enjoy real health, he-man virility, pep and strength" and "weak men" who took it would have virile sex-power restored "almost overnight." Koppel also claimed that his maté would restore all persons using it to good health but he advised a Post Office inspector that he (Koppel) was unable to leave his house because of ill health!

Despite Koppel's claim that he had discontinued advertising his maté product, Solicitor Miles's memorandum stated that there was evidence that Koppel had recently sent literature on it to persons who inquired about a perfume that Koppel advertised under the name of the He-Mo Company. On March 21, 1939, the Postmaster General, acting on Judge Miles's recommendation, issued a fraud order against Koppel's Perez-Maté Company of Brooklyn and its officers and agents as such.

Correspondence

"DOG BITES AND RABIES"

To the Editor:—Your remarks on "Dog Bites and Rabies" (THE JOURNAL, October 7, p. 1434) is a fine example of how one mistake often leads to another.

Cabot in 1899 reported that he saved 91 per cent of the guinea pigs cauterized with nitric acid at the end of twenty-four hours. Rosenau more recently has reported practically 100 per cent of guinea pigs saved by prompt application of nitric acid. In my experience wounds treated with nitric acid heal satisfactorily, and I have never seen one become infected. I believe that the theory that the use of nitric acid causes the spread of infection is not borne out by clinical experience.

Cases of paralysis, some of which have ended fatally following the Pasteur treatment, have been reported in the literature. It should be pointed out that practically all veterinarians who treat rabies have discontinued the use of material prepared by the Pasteur method and are now using material prepared by the Semple method. Since they have so much more experience in treating rabies than do physicians, I believe that their experience should be given consideration. One is forced at least to bring out the fact that vaccine prepared by the Semple method is evidently safer, and the dosage can be more varied according to the clinical indications because one is using a killed rather than an attenuated virus.

L. B. GLOYNE, M.D., Kansas City, Kan.
From the Department of Preventive Medicine,
University of Kansas School of Medicine.

[COMMENT.—In Queries and Minor Notes (this issue, p. 1754) appears an additional discussion of paralysis following rabies vaccination.]

BLOOD SUGAR VERSUS URINARY SUGAR

To the Editor:—In THE JOURNAL June 17 and 24 appears a paper entitled "Blood Sugar versus Urinary Sugar" by Dr. Anthony Sindoni Jr. The author states that:

> In view of the high incidence of disturbed carbohydrate metabolism frequently escaping detection by examination of the urine for sugar and the serious consequences resulting therefrom, blood sugar estimations, fasting and after meals, should be indispensable in early and latent recognition of the blood sugar disturbances:
> (*a*) They should be the governing factor in guiding the insulin dose and diabetic treatment.
> (*b*) Control of the hyperglycemia, not the glycosuria, should be the paramount aim of diabetic treatment.

The estimation of blood sugar levels is indispensable in the recognition of early and latent diabetes, but once the diagnosis has been made there is a question as to the relative value of blood sugar determinations. Diabetes mellitus is a metabolic disturbance not only of carbohydrates but also of proteins and fats, and in evaluating blood sugar levels one must be cognizant of the following points:

1. The glycogenetic and glycogenolytic mechanism of the liver. In diabetes mellitus the glycogenolytic mechanism in particular plays an exaggerated role.

2. That hypoglycemia affects glycogenolysis in the liver. This is an attempt to restore the blood sugar to its former level. Overstimulation of this glycogenolytic mechanism results frequently in hyperglycemia and glycosuria. "Hypoglycemia begets hyperglycemia" (Somogyi).

3. That glycogen is always removed from the liver during periods of hypoglycemia (Cori).

4. That glycogen can be stored in the liver only when the blood sugar level is augmented (Cori).

5. That ketone bodies are formed chiefly in the liver only when glycogen stores of the liver are depleted.

6. That there is a relative constancy of the respiratory quotient of well regulated diabetic patients although there is a wide fluctuation of blood sugars during the twenty-four hour period (Bridge and Winters).

Thus the mechanism that controls the rates of glycogenesis and glycogenolysis must be stabilized to avoid periods of hypoglycemia leading to glycogen depletion in the liver and ketosis. The latter is frequently followed by periods of hyperglycemia and glycosuria. Blood sugar levels within the so-called normal range may represent true hypoglycemic levels for diabetic patients. Hypoglycemic shock has been observed in diabetic patients with sugar content of the blood as high as from 120 to 180 mg. per hundred cubic centimeters of blood (Grafe). This same observation has been made by Mann and Magath in experimental depancreatized hepatectomized dogs.

While the harmful effects of hypoglycemia have been repeatedly demonstrated, those of hyperglycemia without ketosis are highly theoretical. In the management of diabetic patients it is advisable to adjust their diets and dosage of insulin so that a slight trace of glycosuria is maintained throughout the day, thus avoiding the possibility of hypoglycemia consistently. In this day of high carbohydrate diets it is felt that if the diabetic patient constantly utilizes a minimum of 90 per cent of the ingested carbohydrate he is in constant positive carbohydrate balance and is in no danger of ketosis. The respiratory quotients in these patients are high and approach the normal. It is felt that if any one factor is of prime importance in the welfare and management of the diabetic patient it is the state of liver glycogen, and no true indication of the state of liver glycogen can be obtained from blood sugar estimations in diabetes mellitus.

ZOLTON T. WIRTSCHAFTER, M.D., Cleveland.

"DENTAL CARIES AND DOMESTIC WATER SUPPLIES"

To the Editor:—I was much pleased with and interested in the editorial "Dental Caries and Domestic Water Supplies" (THE JOURNAL, September 16, p. 1132). I have had occasion to watch your part in this story of the relation of fluorine to dental conditions.

Only recently I have been shown "An Address on Tooth Culture" by Sir James Crichton-Browne in the *Lancet* of July 2, 1892. On page 7 is a paragraph discussing fluorine and dental caries in which he advises a supply of fluorine for child-bearing women so as to "fortify the teeth of the next generation." An enthusiastic follow-up on Sir James's suggestion at that time might have yielded some human experimental evidence of the causes of mottled enamel, so it is perhaps fortunate that such an application was not then made.

In your own columns may be found at least three items on fluorine and its relation to dental caries, one in the editorial columns Nov. 7, 1931, page 1389, and two in Queries and Minor Notes, Jan. 27, 1934, page 315, and June 9, 1934, page 1964.

An important paper which has received little attention is that of W. D. Armstrong and P. J. Brekhus entitled "Possible Relationship Between the Fluorine Content of Enamel and Resistance to Dental Caries" (*J. Dent. Research* **17**:393 [Oct.] 1938). Their analytic data are evidence from an entirely different angle of the relation of fluorine to dental caries.

My associates and I have experimental evidence contained in a paper to be published in the *Journal of Dental Research* that fluorine added to the diet of pregnant rats results in increased caries resistance in the young. This is an experimental approach which shows that fluorine is responsible for the increased resistance to caries, as it was the sole variable in our procedure. Our work on fluorine has been mentioned in the last three annual reports of the director of the Mellon Institute published in the "News Edition" of *Industrial and Engineering Chemistry.*

It seems therefore that, with three different lines of evidence of this beneficent dental effect of fluorine, namely the Galesburg-Quincy survey of Dean and his associates, the analytic data of Armstrong and Brekhus and our experimental evidence, the case should be regarded as proved.

GERALD J. COX, PH.D., Pittsburgh.
Senior Fellow, Mellon Institute of Industrial Research, University of Pittsburgh.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

PLEURAL PAIN AND PNEUMOTHORAX

***To the Editor:*—A man aged 32 has had artificial pneumothorax treatment of the right lung for the past six years. Previous to collapse therapy he had a pulmonary hemorrhage, the sputum was positive for tubercle bacilli and x-ray studies showed evidence of a moderately advanced lesion of the right lung with no apparent cavities. A short time after artificial pneumothorax was established, fever and cough subsided and the sputum became normal, as it has continued up to the present. Since a supplementary year of rest, the patient has been engaged in a suitable occupation. About six months after institution of pneumothorax, approximately a pint of pleural effusion developed, reaching to the fifth rib anteriorly. The fluid was not removed and remained in the pleural cavity for two years, when it suddenly absorbed, leaving x-ray evidence of "fibrin bodies" at the base of the thorax. The lesion in the lung is apparently healed, and at present and for several years there have been no indications of activity. However, there is this difficulty: If the patient does not have a refill every ten days, the pleural surfaces, which are apparently thickened, rub together and produce a mechanical pleuritis, which causes the temperature to rise as high as 100 or 101 F., with nausea and general malaise, the lung being in approximately 60 to 70 per cent collapse according to fluoroscopic and x-ray examinations. After a refill of from 400 to 500 cc. of air the fever subsides together with the pleural rubbing, and in a day or two all symptoms are gone. The patient is anxious to discontinue pneumothorax treatments because they are no longer needed to control the tuberculosis, but the complication mentioned prevents this. Can any procedures be instituted to alleviate this complication? Are there any studies in the literature on this phase of pneumothorax? What would you suggest as a possible way of discontinuing collapse without having these symptoms? Is it possible that fluid would develop and cause subsidence of symptoms, with eventual absorption permitting reexpansion of the lung? Would a nonirritating oil in small amount such as is used in oleothorax lubricate the pleural surfaces and thus prevent the pleural friction? Any suggestions or references will be greatly appreciated.**

M.D., Pennsylvania.

ANSWER.—From the statements made it is assumed that friction rubs can be elicited over some part of the chest while the lung is still collapsed to 60 or 70 per cent of its volume. Thus it is assumed that the visceral and the parietal pleura are coming in contact at one or more points. After pleurisy with effusion, it seems probable that the pleura contains tuberculous lesions which cause no symptom as long as the lung is under a fairly complete state of collapse. The lesions may be anywhere over the surface of the pleura; that is, they are not necessarily limited to the area over the pulmonary disease. The mechanical effect of the two layers rubbing together in the region of pleural lesions may be sufficient to cause the symptoms. Again, the reexpansion of the lung to 60 or 70 per cent of its volume may result in enough stretching of the visceral pleura to reactivate lesions in it, even though it is not in contact with the chest wall. In fact, too rapid stretching of the pleura in reexpansion may cause its rupture. The pulmonary lesion may also be reactivated by expansion if it is not sufficiently fibrosed.

It is possible that reducing the amount of air of the ten day refills to 100 or 200 cc. might allow the lung to expand more gradually and thus prevent the symptoms, as this amount would be sufficient to reduce the negative intrapleural pressure. If this does not suffice, temporary interruption of the right phrenic nerve so as to paralyze and elevate the diaphragm, thus reducing the size of the pleural cavity, might be given a trial. Following temporary interruption, the nerve fibers regenerate in approximately three months. If this procedure aids in preventing the symptoms, it could be repeated one or more times if necessary, while the lung is being expanded.

The introduction of sterile olive oil or liquid petrolatum up to 100 or 200 cc. might suffice while the lung is reexpanding. Oil has a strong tendency to cause thickening of the pleura since

it is a mild irritant, and therefore it should not be left in the pleural cavity more than a few months at a time. In some cases it causes so much change in the visceral pleura that it becomes impossible for the lung ever to reexpand.

There is the possibility that fluid will form again if the symptoms are permitted to continue, that is, if no air is introduced. In some such cases empyema develops; therefore it would seem safer to employ the procedures outlined.

If from these various procedures no relief from symptoms is experienced as the lung reexpands, it is probably safer to keep the lung collapsed by pneumothorax to the point just below the appearance of symptoms over a longer period, so that in case there are still lesions in the pleura, which are easily activated, they will be given a better opportunity to come under control.

EAGLE FLOCCULATION TEST

***To the Editor:*—Will you please send me information about the Eagle flocculation test for syphilis: 1. What is its present standing as an authoritative laboratory test? 2. In what respects is it superior to the Kahn test on (*a*) untreated and on (*b*) treated patients? 3. In what physical conditions are false positive reactions likely to be found? 4. Do you advise its substitution for the Kahn test or its use as a check on the Kahn test in a laboratory which employs no pathologist?**

M.D. Florida.

ANSWER.—1. The Eagle flocculation test has been designated by the American Serologic Committee as a reliable laboratory procedure for the detection of syphilis.

2. With regard to treated and untreated syphilis, it is impossible at the present time to discuss the superiority of either the Eagle flocculation or the Kahn precipitation test, principally because of the small number of cases on which an authoritative evaluation has been made from this standpoint. Studies thus far, however, seem to give the two tests an approximately equal rating.

3. From the evaluation studies conducted in cooperation with the United States Public Health Service in 1935, and in the experience of various serologists, it has become recognized that flocculation tests in general may give appreciable numbers of false positive results in leprosy, yaws and malaria. In occasional instances false positive results may be encountered in tuberculosis, relapsing fever, infectious mononucleosis, gonococcic, pneumococcic and streptococcic infections, jaundice and malignant conditions and rarely even in a person without recognizable disease.

4. Since the evaluation studies of the United States Public Health Service reveal that both the Eagle and Kahn tests are efficient procedures for the detection of syphilis from the standpoint of sensitivity and specificity when performed in reliable laboratories by properly trained technicians, there should be no valid reason for substituting either test for the other. To use the one procedure as an intralaboratory check on the other, however, obviously would be of merit.

PARALYSIS AFTER RABIES VACCINE

***To the Editor:*—Please give me symptoms, prognosis and treatment of a condition called peripheral paralysis caused by the use of rabies vaccine. All I can find in Meakin's Practice of Medicine is "There is no proven explanation for such, and they are principally of an academic interest." It happens once in 5,000 inoculations. However, it is important from the patient's point of view.**

E. M. Ling, M.D., Hemlock, Mich.

ANSWER.—The latest figures on the occurrence of postvaccinal paralysis from the *Bulletin* of the Health Organization of the League of Nations showed the frequency of paralysis in patients receiving Pasteur antirabic treatment to be thirteen among 121,000 treatments, or one in 10,729. For the entire eight reviews the proportion of accidents has been one in 5,441, or 139 out of 756,000 treatments. It is now readily apparent that killed phenol, heated, and killed ether methods of preparing the vaccine are alike satisfactory regarding the incidence of accident. Nearly all patients have been adults. Two thirds had the onset during treatment and one third soon after its termination. The time of onset has been from eleven to thirty days after the bite for which the treatment was given. This is a much shorter period of incubation than that for rabies. The incubation period of the latter is usually from forty to sixty days. Three clinical types may be distinguished:

Type 1, acute ascending paralysis of Landry. The onset is sudden, with fever, headache, vomiting, severe backache, insomnia and restlessness. The following day the legs are weak and in one or two more days the paralysis is apt to be complete. The sphincters are also paralyzed. Pain, which is usually present in the back, extends upward into the neck and chest, and then the arms become paralyzed. This is followed by pains in the face and paralysis of the throat (bulbar) and face. The prognosis in this type is grave because of bulbar paralysis (respiratory and circulatory arrest). The mortality is about 30 to 40 per cent.

Type 2, dorsolumbar myelitis. The onset is gradual and the fever at first is slight. The legs become completely paralyzed and anesthetic. The sphincters are also involved. The tendon reflexes are lost but occasionally there is a Babinski sign. There are no bulbar signs. Recovery usually occurs in the course of several weeks unless bed sores and urinary tract infection result in lowering the resistance and causing death by sepsis.

Type 3, neuritic form. After a brief febrile period one or more peripheral nerves become involved and cause paralysis. The facial nerve is by far the most frequently concerned. The facial paralysis may be unilateral or bilateral. Other nerves that may become affected are the oculomotor, vagus, radial, ulnar and sciatic. Rapid recovery is usually the rule. The treatment is essentially that of any acute infection, with absolute rest, forcing of liquids and aseptic care to bed sores and urinary abnormalities. The neuritic forms may be treated with local massage and galvanic current after the period of acute involvement. This usually occurs after the second or third week when the temperature is normal. The patient should be placed on an air or water mattress. Foot and wrist drops should have proper immobilization. Vitamins B_1, B_2 and C should be given.

At the present time the various types of paralysis following administration of antirabies vaccine are supposed to be due to the vaccine itself and not to be original rabic infection.

FORDYCE'S DISEASE OF THE VULVA

***To the Editor:*—A young unmarried woman complained of itching of the labia minora. On examination I found a series of closely packed, pinhead size, light yellow papular lesions. The picture to a certain degree resembles Fordyce's disease of the mouth in that it consists of innumerable tiny faintly yellow lesions. There is a certain amount of itch, but it is not intolerable. There is no history in this case of syphilis, diabetes, Trichomonas vaginalis, gonorrhea, masturbation, contraceptives or the local application of irritating ointments. It is the first time that I have ever seen this condition and for all I know it may be common, but I would greatly appreciate your opinion as to the diagnosis.**

William J. Macdonald, M.D., Boston.

ANSWER.—It is probable that this young woman does, indeed, have Fordyce's disease of the vulvar mucous membrane. Fordyce's disease may occur in this situation as well as in the mucous membrane of the lips and mouth. A noninflammatory dermatosis consisting of yellow, discrete puncta on the vulvar mucous membrane and in the mouth would not ordinarily fit in with any other entity. A peculiar type of localized xanthomatosis might be considered, but its presence is not likely. Of course, a biopsy would settle the question. Histologically, masses composed of cells resembling those found in sebaceous glands are found in Fordyce's disease.

Fordyce's disease is devoid of symptoms, the lesions generally being found accidentally. In consequence, the itching present must be accounted for on some other grounds. A moderate amount of pruritus of the vulva and anus is not rare, the causes of which are diverse. Some of these, such as Trichomonas vaginalis, the inquirer has not found present. It is assumed that no local cause for the itching can be found; otherwise that should be corrected.

Pruritus vulvae at the menopause and later may be due to changes in the secretions of the endocrine glands. A general examination should be made to rule out such possible causes as diabetes or nephritis.

If no disease process can be found to account for the itching, local measures may be used for symptomatic relief of the itching. Nothing need be done for the Fordyce's disease. Application of an antipruritic lotion, oil or ointment is indicated. The usual antipruritics are used, such as phenol, menthol and camphor-chloral. These may be employed in somewhat higher concentration than when their general application is required. Applications of moist dressings of water as hot as can be borne may at times tide one over an itching crisis. Painting with a 10 per cent aqueous solution of silver nitrate may be done once or twice a week. The most effective nonspecific agent for vulvar pruritus is the x-ray. Great care should be used not to go beyond a tolerance dose for fear of inducing a radiodermatitis. One fourth of a unit once a week for several weeks is sufficient in many cases. Some recommend local injection of such materials as alcohol and quinine and urea hydrochloride. These measures are seldom indicated and may prove dangerous. A certain experience with them is required. In exceptional cases surgical measures have been employed, but most observers are not in favor of them.

UREA AS DIURETIC

To the Editor:—I would appreciate any information that you may be able to give me as to the use of urea for elimination in cardiac decompensation.

H. S. Rosenberg, M.D., Franklin Square, L. I., N. Y.

ANSWER.—The use of urea as a diuretic in cardiac insufficiency as well as in renal disease was established about twenty years ago in German clinics. The first careful clinical study in the United States was reported in 1925 (Crawford, J. H., and McIntosh, J. F.: *Arch. Int. Med.* **36**:530 [Oct.] 1925). Since then urea has achieved only moderate popularity as a diuretic and in recent years has been largely displaced by the organic mercurials and acid-forming salts. The reasons for this are the limited diuretic effect of urea and its unpleasant taste. The mechanism of its action was recently discussed in Queries and Minor Notes (Urea as Diuretic, THE JOURNAL, June 4, 1938, p. 1945).

It is necessary to give from 30 to 60 Gm. of urea daily to produce diuresis. The 40 or 50 per cent aqueous solution may be diluted with an equal volume of some fruit syrup or taken in carbonated water, beer, tomato juice, coffee or tea. The daily dose is best divided into three portions, given after meals. The salt and fluid intake should be limited in order to favor the removal of edema fluid by the osmotic action of the extra urea. Since urea can readily be ingested as a 20 per cent solution but concentrated by the kidney to only 4 per cent as a maximum, diuresis will occur provided renal function is unimpaired. That urea has no deleterious effect even when taken daily for months or years has been fully demonstrated (Miller, H. R., and Feldman, A.: *Arch. Int. Med.* **49**:964 [June] 1932). It may be advantageous to combine the administration of urea with the use of other diuretics, such as the organic mercurials. Urea is especially helped in preventing the recurrence of cardiac edema after the original dropsy has been controlled by rest, digitalization and ordinary diuretic management. For this purpose a dose of from 15 to 30 Gm. a day may be sufficient. In general, the use of urea will be determined by the patient's gastrointestinal tolerance for the drug.

COCONUT MILK AND DIABETES

To the Editor:—Can you give me any information regarding the value of coconut milk in the treatment of diabetes mellitus or refer me to the literature on the subject?

M.D., New Jersey.

ANSWER.—The composition of coconuts and coconut milk is as follows:

	Carbohydrate, per Cent	Protein, per Cent	Fat, per Cent	Calories per 100 Gm.
Coconuts	27.9	5.7	50.6	590
Coconut milk	4.6	0.4	1.5	34

As may be seen, coconuts are rich in fat and high in calories despite a relatively low carbohydrate content. Coconut milk is low in carbohydrate and in calories. These facts may be responsible for a reputed value of these foods in diabetes. No other information on the subject has been found.

Reference:

Joslin, E. P.: Treatment of Diabetes Mellitus, Philadelphia, Lea & Febiger, 1937, p. 681.

LEAD CONTENT OF CRAYON CHALK

To the Editor:—Recently there have been articles commenting on lead poisoning resulting from the use of chalk containing lead chromate. In this connection some of the crayon companies state that their chalk is nontoxic. Have you any data proving whether or not chalk may have small amounts of lead and still be nontoxic? As I understand lead poisoning, lead is cumulative. Therefore a person exposed to lead, either by inhaling dust or by nibbling chalk containing lead even though in small amounts, would possibly be accumulating enough lead actually to cause poisoning. The points that I would like to have answered are: What amount of lead in chalk would be toxic, or would chalk have to be absolutely free of lead to be considered nontoxic?

Malvin J. Nydahl, M.D., Minneapolis.

ANSWER.—In 1937, C. M. Jephcott (Lead in Certain Coloured Chalks and the Danger to Children, *Canad. Pub. Health J.* **28**:391 [Aug.] 1937) reported finding high concentrations of lead chromate in yellow, orange and green crayons but no lead in other colored chalks. Chalks recently analyzed by the Massachusetts State Division of Occupational Hygiene, under the direction of Manfred Bowditch, were found to contain between 2.2 and 18.7 per cent of lead. These high percentage chalks would seem to be definitely undesirable for children to use, particularly because of the dust which they produce. Crayon manufacturers are now cognizant of this risk, and it is believed that this high lead content already has been eliminated from some colored chalks. One cannot say exactly how much lead would be permissible in that chalk. The factor of importance is the amount of lead present in the air which is breathed. A larger percentage of lead in chalk would be safe if blackboards were cleaned with water rather than with the dust-producing eraser. The usual safe limit of daily lead absorption is stated to be about 2 mg. a day in breathed air. Somewhat larger amounts could be taken by mouth without deleterious effects. Therefore chalk would not have to be absolutely free of lead to be considered nontoxic, but it ought not contain a large percentage of lead. Certainly the high percentage now found in some chalk should be reduced, no matter what chemical compound of lead is employed.

EFFECT OF SULFANILAMIDE ON GONOCOCCI

To the Editor:—It has repeatedly been stated that the use of sulfanilamide in the treatment of gonococcic infections may alter the morphologic appearance of the gonococcus. A detailed report of the changed appearance of the sulfanilamidized gonococcus as observed microscopically would be appreciated.

Heinrich Lamm, M.D., La Feria, Texas.

ANSWER.—Under sulfanilamide therapy the slide characteristics of both gonococci and secondary organisms become unusually irregular. Size, shape, relationship to pus and epithelial cells and to a lesser extent staining characteristics change. The organisms may become unrecognizable and confused with one another. There are more extracellular organisms and the pus cells confusingly contain what may be a single organism or pair of organisms, a fragment of nuclear material or merely débris. The gram-negative short coliform bacilli in the early division stage can easily pass for gonococci. They may be intracellular.

The most reliable diagnostic criteria are cultural. Atypical gonococci always revert to type when implanted on suitable soil, whether it is a laboratory medium or the urinogenital epithelium.

POSSIBLE SCIATIC OR PERINEAL HERNIA

To the Editor:—Please suggest possible diagnoses or diagnostic procedure in the following case: A white woman aged 36, 5 feet 6 inches (168 cm.) tall, weighing 235 pounds (106.6 Kg.), complains of a large "lump" present on the upper outer quadrant of the left buttock. This "lump" is transient, appearing within a space of a few hours, persisting for several hours or days and finally disappearing as rapidly as it came. It has been present intermittently for the past six months. The time of appearance does not seem to be influenced by activity. There is some pain associated with this mass—at times referred medially to the region of the sacroiliac joint and at other times anteriorly to the groin. There is moderate discomfort on walking because of its size. The past history reveals three normal pregnancies, no miscarriages and no previous infectious diseases. She has complained of some pain in the left thigh of an indefinite nature for years. About six months before this swelling made its appearance she had a large carbuncle on the left knee. This is entirely healed at present. Physical examination reveals nothing of interest other than marked generalized obesity. On the upper outer quadrant of the left buttock is a swelling the size of a large grapefruit. There is no discoloration or fluctuation. It is apparently a muscular swelling and is only slightly tender. The upper edge reaches the crest of the ilium posteriorly. The temperature, pulse, blood pressure, urine and blood count are normal and the Wassermann reaction is negative. X-ray examination of the hip joint and adjacent structures revealed no pathologic condition. The patient was seen a day later. She stated that the mass had disappeared during her sleep the night before. Examination then showed no deviation in the normal contour of the buttock. About two days later, however, the patient returned with the mass present again; it had appeared that morning while she was baking and looked essentially the same as before.

M.D., Pennsylvania.

ANSWER.—This is an unusual case and certainly warrants careful study. The transient nature of the swelling excludes neoplasms of the soft part. Moreover, x-ray examination excludes neoplasms originating from the bone. It would seem that this swelling must be either some type of hernia or a fluid collection which has an hour-glass shape permitting the fluid to go back and forth from one to the other of two compartments. Hernia seems the more likely explanation, although the situation high on the buttock is hard to explain.

About thirty cases of sciatic hernia have been reported. In this condition the hernia emerges from the pelvis through the sacrosciatic notch and protrudes into the folds between the buttock and the leg (Andrews Edmund, in Textbook of Surgery Frederick Christopher, editor, Philadelphia, W. B. Saunders Company, 1936). This type of hernia is best repaired by laparotomy, and great care should be exercised to avoid injury to the sacral plexus.

In perineal hernia the herniation is through the pelvic floor, but in the posterior type of this hernia it emerges behind the transverse perineal muscle. It is possible that one of these two rare types of hernia may explain the condition. Help to substantiate the diagnosis of hernia might be obtained by the x-ray film showing gas bubbles in the soft part as of loops of small intestine. Or, if an x-ray film of the gastrointestinal tract could

be taken when the swelling is present it might show barium-filled loops outside the pelvis. Aspiration would seem to be somewhat risky.

A rupture of the insertion of the gluteus muscle with bunching up of this muscle toward the crest of the ilium might be considered, but this would be constantly present with every effort to contract the gluteus.

After all other efforts at diagnosis have been exercised, this case would warrant surgical exploration from the outside.

DIGITALIS AND EPHEDRINE

To the Editor:—**In The Journal, May 16, 1931, Johnson and Gilbert advised that "when digitalis is being used for the heart, ephedrine should not be used or with extreme caution." Has this been substantiated by other observers? Luten in his book The Clinical Use of Digitalis (Springfield, Ill., Charles C. Thomas, 1936) mentions Johnson and Gilbert's statement, page 127.**

H. B. Aitkens, M.D., Le Center, Minn.

ANSWER.—The work of Johnson and Gilbert has neither been confirmed nor denied. It would only rarely be of importance clinically. Clinical doses of digitalis seldom reach 50 per cent of the minimal lethal dose. The lethal dose of ephedrine in the anesthetized dog is 70 mg. per kilogram, but in the unanesthetized dog it is about 40 mg. per kilogram. It is improbable that any clinical dose of ephedrine could possibly approach half this figure. On the other hand, if enough digitalis had been given to increase the irritability of the cardiac muscle up to a certain point, a moderate dose of ephedrine might further increase irritability and result in ventricular fibrillation and death. Digitalis, of course, should never be given to such a point.

The experimental work indicated a definite synergistic action between the two drugs. While fatal results clinically would be unlikely, except with a dosage of either drug which would never be necessary and which should never be used, it is just as well to bear in mind that experimental work does show a definite synergism, and they should be used with a moderate degree of caution.

EFFECT OF HIGH INTRACRANIAL PRESSURE ON PULSE AND BLOOD PRESSURE

To the Editor:—**What influence does a rise in intracranial pressure of from 400 to 800 mm. of water have on the pulse rate and blood pressure? The literature is contradictory. Do you know any references to reports of cases, traumatic or otherwise, characterized by (1) a high cerebrospinal fluid pressure (but not high enough to approach the level of the systolic blood pressure), a lowered pulse rate and a rising blood pressure and (2) a return of pulse rate and blood pressure to normal when the intracranial pressure has been sufficiently reduced?**

M.D., New York.

ANSWER.—In the presence of increased intracranial pressure the pulse is usually, but not always, slow until the breaking point of compensation, when it becomes increasingly rapid. In many instances, however, the pulse rate is not affected. The blood pressure is usually not altered but at times is increased slightly when the rise in pressure is sudden or rapid. The bradycardia will return to normal within a week or two after relief of intracranial pressure. There seem to be no precise records on this point, but the facts as given are well recognized in all clinics where intracranial pressure is commonly seen in the presence of tumors or cranial trauma.

DERMATITIS FROM ROCK WOOL

To the Editor:—**Do you have any information concerning a dermatitis occurring among insulators who handle rock wool? What type of dermatitis is most common and is there definite evidence that the rock wool is the etiologic factor? What have been the most successful means of preventing this dermatitis? In other words, if there have been any reports of such a dermatitis I would appreciate learning as much about it as possible.**

Ralph E. Jones, M.D., Chicago.

ANSWER.—Rock wool, slag wool, slagbestos or mineral wool is made by blowing air and steam through iron blast-furnace molten slag or through natural siliceous limestone or calcareous shale rocks when in a molten state. This converts the slag or rock into fine threads like cotton wool which are insect and fire proof. The product is used as an insulating material, a filtering medium, a covering for steam pipes and for packing.

Occupational dermatitis attributed to rock wool and confirmed by positive patch tests has previously been reported to the Office of Dermatoses Investigations of the U. S. Public Health Service. The irritating properties of this substance are said by R. Prosser White (The Dermatergoses or Occupational Affections of the Skin, ed. 4, London, H. K. Lewis Company, Ltd., 1934) to be due to its content of quicklime, 10 per cent, and calcium sulfide, 5 per cent, as well as to spicules which it contains. Its dust is said to be irritating also to the mucous membranes of the nose and eyes.

Since its alkaline content and the spicules it contains are said to be the causes of dermatitis from this material, it would seem that the wearing of rubber gloves and dust-proof clothing, with frequent changes of work clothes and cleansing shower baths after work, would offer the best protection against this occupational hazard to the skin. The use of protective ointments, especially those which are said to give protection against alkalis, may also be of benefit.

MIGRATION OF TESTES

To the Editor:—**A boy now 10 years of age was seen shortly after birth, at which time he had an undescended right testis with the left testis in the scrotum. A few months later there was torsion of the right testis with gangrene, requiring its removal. I saw the boy recently and the left testis was still in the scrotum and was about the size of a pea. The mother showed me his brother, aged 7 years, whom I also saw at birth, and I know that both testes were normal at that time and were in the scrotum. When I saw the boy yesterday neither testis could be palpated and there was no evidence of any hernia. The youngest son, aged 4 years, has a small left testis with no evidence of a right testis. I know likewise that at birth he had both testes in the scrotum. I should like advice as to the prognosis and treatment.**

M.D., Massachusetts.

ANSWER.—With regard to the boy aged 10 years who had one testis removed for gangrene because of torsion, as long as the left testis is in the scrotum one should do nothing and merely keep the boy under observation. It would be desirable to have the boy see his physician once a year.

With regard to the boy aged 7 years, in whom the testes were normal and in the scrotum at birth, it is stated that the physician saw the boy recently and neither testis could be palpated. It is well known that in some patients the testes do retract and move up and down—a phenomenon that has been recognized for a long time. It is failure to recognize this which leads to erroneous diagnoses. Some of these patients are prepared for operation for undescended testes, and just before the operation is started the testes are found in the scrotum. In several observed instances in which the testes moved up and down they ultimately found their way into the scrotum and stayed there.

The same explanation will suffice for the boy aged 4 years. He should be kept under close observation. Some patients who belong to this group and in whom this condition is not recognized are given long courses of endocrine treatment and the descent of the testes is erroneously ascribed to the use of the endocrine substance.

To sum up, these boys should report to the physician's office once a year. Nothing should be done in a surgical way and certainly they should not be given endocrine therapy.

TABES WITH NEGATIVE SEROLOGIC REACTIONS OF THE BLOOD AND SPINAL FLUID

To the Editor:—**Is it possible to have syphilis of the central nervous system with repeatedly negative Wassermann and Kahn reactions of the blood since childhood and a spinal fluid in which the cell count is 1 and the colloidal gold curve and the Wassermann reaction are negative and globulin normal? The patient has a fixed, dilated right pupil, the knee jerks are absent, the Romberg sign is absent, there are questionable saber shins, there is a backache with questionable root-pain type of radiation and she is married to a man who has tabes but who was treated moderately before marriage.**

M.D., New Jersey.

ANSWER.—It is possible, in fact it is noted quite frequently in a syphilologist's practice, that patients with clinical signs of tabes dorsalis will have negative reactions of the blood and spinal fluid. These are known as "burnt out tabetics" and the negative serologic reactions may have developed in one or two ways, either as the result of treatment or spontaneously. The latter group are less numerous and, although these serologic negative reactions developed without treatment, the use of arsphenamine and bismuth compounds does not control the persistent symptoms such, for example, as the neuritis of tabes. The evidence presented in the inquiry is not enough on which to base a conclusive diagnosis of tabes, since some neurologists believe that such suggestive clinical manifestations might be the residue of a nonsyphilitic inflammatory lesion of the central nervous system. The fact that the husband has tabes increases the possibility that the patient under discussion may have had syphilis. Even so there is little that can be done for her, since antisyphilitic therapy in such cases offers but slight relief.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

Examinations of state and territorial boards were published in THE JOURNAL, October 28, page 1663.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: Parts I and II. Medical centers having five or more candidates desiring to take the examination, Feb. 12-14. Part III. Chicago and New York, January. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th Street, Philadelphia.

SPECIAL BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: An Affiliate of the American Board of Surgery. *Written.* Part I. Various places throughout the United States and Canada, March 28. Sec., Dr. Paul M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Various sections of the United States, Feb. 19. Formal application must be received on or before Jan. 1. Sec., Dr. William S. Middleton, 1301 University Ave., Madison, Wis.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *General oral and pathologic examinations (Part II) for all candidates (Groups A and B)* will be conducted in Atlantic City, N. J., June 8-11. *Applications for admission to Group A, Part II examinations must be on file not later than March 15.* Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh (6).

AMERICAN BOARD OF OPHTHALMOLOGY: *Written.* Various cities of the United States and Canada, March 2. (The only written examination in 1940.) Oral. New York, June 8-10. *Formal applications must be received before Jan. 1.* Sec., Dr. John Green, 6830 Waterman Ave., St. Louis.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, June 3-5. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PATHOLOGY: Memphis, Nov. 22-23. Sec., Dr. F. W. Hartman, Henry Ford Hospital, Detroit.

AMERICAN BOARD OF PEDIATRICS: New York, April 30 and May 1. Kansas City, Mo., preceding the Region III meeting of the American Academy of Pediatrics, Seattle, June 2. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York, December 18-19. Sec., Dr. Walter Freeman, 1028 Connecticut Ave. N.W., Washington, D. C.

AMERICAN BOARD OF RADIOLOGY: Atlanta, Ga., Dec. 9-11. Sec., Dr. Byrl R. Kirklin, 102-110 Second Avenue S.W., Rochester, Minnesota.

AMERICAN BOARD OF SURGERY: Part II. Atlanta, Nov. 15. *Will include candidates living in the South only.* Sec., Dr. J. Stewart Rodman, 225 S. 15th St., Philadelphia.

AMERICAN BOARD OF UROLOGY: Chicago, Feb. 9-11. (The only examination session to be held in 1940.) *Case reports must be submitted not later than November 9.* Sec., Dr. Gilbert J. Thomas, 1009 Nicollet Ave., Minneapolis.

Missouri June Report

Dr. Harry F. Parker, secretary, State Board of Health of Missouri, reports the written examination held at St. Louis, June 1-3, 1939. The examination covered fifteen subjects. An average of 75 per cent was required to pass. One hundred and ninety-nine candidates were examined, all of whom passed. Thirteen physicians were licensed by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Howard University College of Medicine		(1937)	78.1
Northwestern University Medical School	(1938) 78.1,	(1939)	84
Rush Medical College		(1938)	87.8
Harvard Medical School		(1936)	83.7
St. Louis University School of Medicine	(1938) 84.6, (1939) 76, 76.8, 78, 78.6, 78.7, 78.8, 78.9, 79, 79.1, 79.4, 79.4, 79.5, 79.8, 79.9, 80, 80.1, 80.3, 80.8, 81.2, 81.2, 81.2, 81.2, 81.3, 81.4, 81.4, 81.4, 81.4, 81.6, 81.6, 81.7, 81.8, 81.9, 82, 82, 82, 82.1, 82.2, 82.3, 82.3, 82.3, 82.4, 82.4, 82.4, 82.6, 82.6, 82.6, 82.6, 82.7, 82.8, 82.9, 83, 83, 83.2, 83.3, 83.4, 83.4, 83.5, 83.6, 83.6, 83.7, 83.7, 83.8, 83.8, 84, 84, 84.1, 84.2, 84.3, 84.4, 84.4, 84.4, 84.6, 84.6, 85, 85, 85.1, 85.3, 85.5, 85.7, 85.7, 85.8, 86, 86, 86, 86, 86.2, 86.5, 86.5, 86.6, 86.6, 87.2, 88, 89.6	(1937)	83,
Washington University School of Medicine	(1939) 77.5, 78.1, 78.4, 79, 79.5, 79.6, 79.8, 79.8, 80, 80.2, 80.3, 80.4, 80.5, 80.6, 80.6, 80.6, 80.7, 80.7, 80.8, 81, 81, 81, 81, 81.2, 81.2, 81.3, 81.4, 81.6, 81.8, 81.8, 82, 82.1, 82.2, 82.4, 82.4, 82.4, 82.4, 82.6, 82.6, 82.6, 82.7, 82.7, 82.9, 83, 83, 83.1, 83.1, 83.2, 83.2, 83.2, 83.2, 83.2, 83.2, 83.4, 83.4, 83.6, 83.6, 83.6, 83.8, 83.8, 83.8, 83.9, 84, 84, 84.1, 84.2, 84.2, 84.5, 84.8, 84.9, 85, 85.2, 85.4, 85.7, 86, 86.1, 86.1, 86.4, 86.6, 86.6, 86.6, 86.7, 86.9, 87, 87.4, 87.8, 88.3, 88.6, 88.8	(1937)	83.8,
Medical College of the State of South Carolina		(1935)	81
Meharry Medical College		(1935)	78.6
University of Texas School of Medicine		(1938)	84.6
University of Wisconsin Medical School		(1938)	79.9
University of Toronto Faculty of Medicine		(1936)	87.6
Medizinische Fakultät der Universität Wien		(1902)	75.6
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin		(1924)	76.2
Regia Università degli Studi di Genova Facoltà di Medicina e Chirurgia		(1936)	75.6
Regia Università di Napoli Facoltà di Medicina e Chirurgia		(1936)	80.5

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine		(1938)	Colorado
Georgetown University School of Medicine		(1937)	New Mexico
Loyola University School of Medicine		(1929)	Illinois
Northwestern University Medical School		(1938)	Kansas
Rush Medical College		(1937)	Illinois
University of Illinois College of Medicine		(1937)	Illinois
University of Kansas School of Medicine		(1933), (1935)	Kansas
Johns Hopkins University School of Medicine		(1935), (1938)	Maryland
University of Nebraska College of Medicine		(1937)	Nebraska
University of Oklahoma School of Medicine		(1938)	Maryland
Meharry Medical College		(1937)	Tennessee

Ohio June Examination

Dr. H. M. Platter, secretary, Ohio State Medical Board, reports the oral, written and practical examination held at Columbus, June 6-9, 1939. The examination covered ten subjects and included eighty questions. An average of 75 per cent was required to pass. Three hundred and twenty-six candidates were examined, 314 of whom passed and twelve failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Georgetown University School of Medicine		(1938)	82.1, 84.6
George Washington University School of Medicine	(1939) 83.1, 84.6, 85.7	(1938)	82.5,
Loyola University School of Medicine	(1939, 2)*	(1939, 6)	83,
Northwestern University Medical School		(1939)	83.4
Rush Medical College	(1938) 83.3, 83.7, 83.8	(1937)	83.7,
The School of Medicine of the Division of Biological Sciences		(1938)	86.3, (1939) 86.9
University of Illinois College of Medicine		(1918)	82.7
University of Louisville School of Medicine		(1938)	82.5
Harvard Medical School	(1936) 78.5, (1938) 81.9, (1939) 85.6	(1935)	85.8,
Tufts College Medical School		(1937)	83.9
University of Minnesota Medical School		(1936)	86.2
Washington University School of Medicine		(1938)	88
Creighton University School of Medicine		(1938) 84.1,	(1939) 83.8
Columbia University College of Physicians and Surgeons		(1935)	83.9
Cornell University Medical College		(1938)	87.4
New York University College of Medicine		(1939)	82.9
University of Rochester School of Medicine	(1939) 81.7, 82.4, 84.9, 86.4, 87.6, 88.4, 88.5	(1938)	86,
Eclectic Medical College	80.2, 80.5, 80.6, 81.3, 81.7, 81.8, 81.9, 82.1, 82.2, 82.5, 82.7, 82.8, 82.9, 83.6, 83.9, 84.1, 84.7, 84.8, 85.3, 85.5, 85.5, 85.6, 85.7, 85.7, 85.8, 86, 86.6, 87.6, 87.6, 87.7, 87.9, 88.5, 88.6, 89.1, 89.1	(1939)	79.8,
Ohio State University College of Medicine	80.1, 80.4, 80.4, 81.5, 81.5, 81.7, 81.8, 81.8, 81.9, 82, 82.2, 82.3, 82.3, 82.6, 82.7, 82.7, 82.8, 82.8, 82.9, 83.1, 83.2, 83.2, 83.3, 83.4, 83.5, 83.6, 83.7, 83.8, 83.9, 83.9, 84.1, 84.1, 84.2, 84.2, 84.3, 84.4, 84.5, 84.5, 84.5, 84.6, 84.6 84.6, 84.8, 85, 85.1, 85.2, 85.2, 85.4, 85.5, 85.5, 85.6, 85.6, 85.7, 85.8, 85.8, 85.9, 85.9, 86.2, 86.3, 86.3, 86.9, 86.9, 86.9, 86.9, 87, 87.2, 87.2, 87.3, 87.4, 87.4, 87.4, 87.4, 87.5, 87.7, 87.7, 87.9, 88.1, 88.5, 89.4	(1939)	79.9,
University of Cincinnati College of Medicine	78.6, 79.3, 79.5, 79.7, 79.9, 80.1, 80.3, 80.3, 81.1, 81.1, 81.1, 81.3, 81.5, 81.5, 81.6, 81.6, 81.8, 81.9, 82.1, 82.1, 82.1, 82.4, 82.5, 82.6, 82.7, 82.8, 82.9, 83, 83.1, 83.3, 83.3, 83.5, 83.5, 83.7, 83.9, 84, 84.1, 84.3, 84.4, 84.4, 84.4, 84.6, 84.7, 84.8, 85.1, 85.1, 85.2, 85.2, 85.6, 85.7, 85.8, 85.8, 85.9, 85.9, 86.2, 86.2, 86.2, 86.5, 86.8, 86.9, 87.5, 87.6	(1939)†	77.6,
Western Reserve University School of Medicine	81.4, 81.6, 81.7, 82.2, 82.3, 82.4, 82.4, 82.6, 82.6, 82.6, 82.6, 82.6, 82.7, 82.7, 82.8, 82.9, 83.1, 83.1, 83.2, 83.3, 83.4, 83.7, 83.7, 83.8, 83.9, 83.9, 84.2, 84.3, 84.5, 84.5, 84.6, 84.6, 84.6, 84.6, 84.7, 84.7, 84.7, 84.8, 84.9, 84.9, 85, 85, 85, 85.1, 85.2, 85.4, 85.4, 85.5, 85.7, 85.7, 85.8, 86.2, 86.4, 86.5, 86.9, 87.6, 87.7, 87.9, 88.4, 89.6	(1939)	80.1,
Jefferson Medical College of Philadelphia	83.5, 89.4	(1938)	81,
Hahnemann Med. College and Hospital of Philadelphia		(1938)	84.3
University of Pennsylvania School of Medicine		(1938)	81.5, 82.2
University of Wisconsin Medical School	(1938) 82.8, 84.9	(1937)	84.6,
McGill University Faculty of Medicine	(1938) 83,	(1939)	83.5
Medizinische Fakultät der Universität Wien	(1921) 79.7, (1925) 77.7, (1930) 79.1, (1935) 83.9, (1937) 82.4	(1911)	74.6,
Deutsche Universität Medizinische Fakultät, Prag		(1934)	81.7
Université de Paris Faculté de Medicine		(1926)	75.9
Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg		(1924)	77.4
Friedrich-Alexander-Universität Medizinische Fakultät, Erlangen		(1923)	80.5
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin	(1913) 75.1, (1923) 77.5, (1927) 79.6,	(1935)	82.6
Julius-Maximilians-Universität Medizinische Fakultät, Würzburg		(1915)	76.3
Kaiser-Wilhelms-Universität Medizinische Fakultät, Strassburg		(1918)	75
Ludwig-Maximilians-Universität Medizinische Fakultät, München		(1906)	78.2
Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn	(1926) 74.9, 81,	(1934)	83.8
Universität Heidelberg Medizinische Fakultät		(1932)	80.5
Magyar Királyi Tisza-István-Tudományegyetem Orvosi Fakultasa, Debrecen		(1932)	83.4

Universität Basel Medizinische Fakultät	(1936)	80.4, 80.4
Universite de Lausanne Faculté de Médecine	(1936)	82

School	FAILED	Year Grad.	Per Cent
Medizinische Fakultät der Universität Wien		(1924)	74.1
Université de Montpellier Faculté de Médecine		(1933)	73.3
Albertus-Universität Medizinische Fakultät, Königsberg		(1922)	73.9
Christian-Albrechts-Universität Medizinische Fakultät, Kiel		(1900)	72.9
Friedrich-Wilhelms Universität Medizinische Fakultät, Berlin		(1911) 73.5, (1929)	74.5
Ludwig-Maximilians-Universität Medizinische Fakultät, München		(1912)	72.4
Vereinigten Friedrichs-Universität Medizinische Fakultät, Halle-Wittenberg		(1921)	73.2
Regia Università degli Studi di Genova Facoltà di Medicina e Chirurgia		(1924)	72.6
Regia Università degli Studi di Modena Facultà di Medicina e Chirurgia		(1934)	70.9
Regia Università degli Studi di Roma Facoltà di Medicina e Chirurgia		(1936)	68.8
Université de Lausanne Faculté de Médecine		(1938)	72

* These applicants have completed the medical course and will receive the M.D. degree on completion of internship. Licenses have not been issued.

† These applicants have received the M.B. degree and will receive the M.D. degree on completion of internship.

Virginia June Examination

Dr. J. W. Preston, secretary, Virginia State Board of Medical Examiners, reports the written examination held at Richmond, June 21-23, 1939. The examination covered eight subjects and included eighty questions. An average of 75 per cent was required to pass. One hundred and three candidates were examined, 102 of whom passed and one failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
George Washington University School of Medicine		(1938)	82
Howard University College of Medicine		(1938)	80
Tulane University of Louisiana School of Medicine		(1917)	76
Harvard Medical School		(1939)	80
Hahnemann Med. College and Hospital of Philadelphia		(1939)	79
Jefferson Medical College of Philadelphia		(1939)	84
Temple University School of Medicine		(1939)	84
Medical College of Virginia (1936) 88, (1939) 75, 78, 78, 79, 80, 80, 80, 81, 82, 82, 82, 82, 82, 82, 83, 83, 83, 84, 84, 85, 85, 85, 85, 85, 86, 86, 86, 86, 86, 87, 87, 87, 87, 87, 88, 88, 88, 89, 90, 91			
University of Virginia Department of Medicine (1938) 79, (1939) 76, 77, 78, 78, 79, 80, 80, 80, 81, 81, 81, 81, 82, 82, 82, 82, 82, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 83, 84, 84, 84, 84, 84, 84, 84, 84, 84, 84, 85, 85, 85, 85, 85, 85, 85, 86, 86, 87, 90			
Queens University Faculty of Medicine		(1928)	77

School	FAILED	Year Grad.	Per Cent
Howard University College of Medicine		(1938)	73.5

Thirty-four physicians were licensed by reciprocity and seven physicians were licensed by endorsement on February 10 and June 23. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1937)	Arkansas
George Washington University School of Medicine		(1926) (1934)	New York, Maryland
Georgetown University School of Medicine		(1916), (1937)	Dist. Colum.
Northwestern University Medical School		(1932)	Wisconsin
University of Louisville School of Medicine		(1926), (1935)	Kentucky
University of Maryland School of Medicine and College of Physicians and Surgeons		(1917), (1937, 2)	Maryland
Johns Hopkins University School of Medicine		(1930), (1935)	Maryland
Harvard Medical School		(1933)	New York
Washington University School of Medicine		(1934)	Illinois
Columbia Univ. College of Physicians and Surgeons		(1935)	New York
Long Island College of Medicine		(1931)	S. Dakota
University and Bellevue Hospital Medical College		(1904) (1931)	New York, District of Columbia
Duke University School of Medicine		(1932)	W. Virginia
University of Cincinnati College of Medicine		(1938)	Ohio
Western Reserve University School of Medicine		(1937)	Ohio
Hahnemann Medical College and Hospital of Philadelphia		(1918) Dist. Colum., (1936)	W. Virginia
Temple University School of Medicine		(1910)	Penna.
University of Pennsylvania School of Medicine		(1917)	Penna.
Medical College of the State of South Carolina		(1912)	S. Carolina
Meharry Medical College		(1926) (1938)	Missouri, Tennessee
University of Tennessee College of Medicine		(1922), (1935)	Tennessee
Medical College of Virginia		(1938)	N. Carolina
University of Wisconsin Medical School		(1936)	Wisconsin
McGill University Faculty of Medicine		(1922)	Penna.

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Georgetown University School of Medicine		(1935)	N. B. M. Ex.
Harvard Medical School		(1935)	N. B. M. Ex.
Temple University School of Medicine		(1936)	N. B. M. Ex.
University of Tennessee College of Medicine		(1929)	U. S. Navy
Medical College of Virginia		(1917)	U. S. Navy
McGill University Faculty of Medicine		(1936)	N. B. M. Ex.
University of Oxford School of Medicine		(1920)	Australia

Book Notices

Treatment in General Medicine. Edited by Hobart A. Reimann, M.D., Magee Professor of Practice of Medicine and Clinical Medicine, Jefferson Medical College, Philadelphia. In Three Volumes and Desk Index. Cloth. Price, $30 per set. Pp. 895; 1001-1896; 2001-2834, with illustrations; 107. Philadelphia: F. A. Davis Company, 1939.

Recognizing that advancement of modern medicine has made medical problems so highly specialized that it is no longer possible for one individual to cover completely any single medical field, Dr. Reimann has developed a system of therapeutics in which distinguished specialists consider various phases of the treatment of individual diseases. Since treatment must depend on knowledge of cause and on symptoms, space is given to these subjects and also to considerations of other factors in disease intimately associated with treatment. It is recognized that psychotherapy is an intimate part of all the treatment of disease, and special attention is also given to this aspect of medical care. Finally, the volume includes discussions of minor surgical, gynecologic and obstetric treatment, as well as a chapter of the conditions associated with old age. The volumes are important also because they emphasize standardized and controlled treatment. Thus the remedies concerned are those available through the United States Pharmacopeia, the National Formulary and New and Nonofficial Remedies. In line with the recommendations of standard therapy, the work begins with a foreword by the editor of THE JOURNAL discussing the basis of scientific therapy. Thereafter the volume takes up, in the usual order, the treatment of infectious conditions, parasitic diseases, the heart, the blood vessels, the gastrointestinal tract and the genitourinary tract. There are excellent discussions of prophylaxis. Selected bibliographies indicate to the reader the places for further detailed study. The list of contributors includes many of the best known names in modern medicine. In the final volume there are chapters on technical therapeutic procedures, irradiation, all of the various forms of physical and occupational therapy, and finally chapters on rest and the use of spas. This is a modern, direct, useful system of treatment.

The Surgical Treatment of Hypertension. By George Crile. Edited by Amy Rowland. Cloth. Price, $4. Pp. 239, with 52 illustrations. Philadelphia & London: W. B. Saunders Company, 1938.

This work is a conglomeration of theories, facts, fallacies, scientific and pseudoscientific observations and unwarranted assumptions, welded together loosely in an unconvincing manner and in a style in which repetition and reiteration are apparently used to bolster the faltering argument. The constant assumption of unproved facts and the wide digressions into far flung fields of investigation, fields which are evidently unfamiliar to the author, confuse rather than clarify the subject. Many of the basic principles on which the flimsy superstructure is built are false or are erroneously interpreted. Controversial points are assumed to be definitely established. One is impressed with the apparent superficial knowledge of the author regarding much of present day physiologic concepts and especially of the functions and modus operandi of the sympathetic nervous system.

Considerable space is devoted to a comparison of the brains, thyroids, adrenals and celiac ganglions of fish, python, alligator, lion, tiger and man in the hope of promulgating a general law that the size of these organs determines the oxygen requirements and speed of oxygen utilization. "The size of the brain and the thyroid gland, the adrenal glands, the sympathetic system, the celiac ganglia, the aortic plexus, the heart, the volume of blood, the richness of the capillaries—all of these would be governed by a general law of energy release." It takes considerable imagination after reading the entire book to see just what this has to do with hypertension in man. However, except in small mammals and birds, Crile finds, "man is mechanized for the highest energy requirements of any animal on land or in the sea."

The next chapter indicates that it is a pathologic physiology of this mechanism governing the rate of oxidation and the circulation which produces hypertension. Later he suggests that only individuals who have abnormally large celiac ganglions and plexuses can have hypertension.

Numerous errors in his concept of the anatomic physiology of the sympathetic system are evident. Perhaps the most striking one is his evident belief that the sympathetic impulses to the entire arterial system are made directly to the aorta from the overlying celiac ganglion. "This principle of synaptic functions is found in the sympathetic control of the vascular system by the centralization of all the synaptic functions into one major end-plate, which is strapped down on the aorta with such a strength of cordage that in the midst of every kind of fighting, running, etc., the function would be secure, to the end that power could be discharged into the great vascular tree with the suddenness of a bullet."

The theories of the surgical treatment of essential hypertension are discussed at considerable length but apparently without a firm grasp of the basic principles involved. Other diseases of the sympathetic nervous system are considered and he states that "each of these diseases—hyperthyroidism, neurocirculatory asthenia, Raynaud's disease—are abated or cured by adrenal denervation or celiac ganglionectomy."

The technic of celiac ganglionectomy is fully described and illustrative cases are given in detail. There is also a somewhat inaccurate historical summary of the various surgical procedures used in the treatment of hypertension.

Three chapters by other members of the clinic are included: types of arterial hypertension and their recognition by Ernstein, the ocular examination of the patient with hypertension by Ruedemann, and the renal lesions in essential hypertension by McDonald. Ruedemann's chapter is well worth reading. In summary he states that adrenalectomy exerts only a temporary effect on blood pressure, that denervation of the adrenals is little better, that division of the splanchnic nerves with denervation of the adrenals produces a more lasting effect, and that the best result in his hands is secured by bilateral celiac ganglionectomy and adrenal denervation.

Medical Opinions on War. Published on behalf of the Netherlands Medical Association (Committee for War-Prophylaxis). Paper. Pp. 72, New York, Amsterdam & London: Elsevier Publishing Company, [n. d.]

This pamphlet, published on behalf of the Netherlands Medical Association, is a compilation of brief statements by fifteen physicians representing England, Germany, the United States, the Netherlands and Sweden, together with a letter to the statesmen signed by 340 leading psychiatrists from twenty nations, representing Europe, Asia and North and South America. It sets forth the conviction of the psychiatrists that war is a psychologic problem and that the solution must be along psychologic and psychiatric lines. The titles include such significant ones as war and human nature; the war problem—a psychologic approach; psychology and peace; imagination and war prophylaxis; biologic considerations in the prevention of war; women and war (by a woman physician); war and mass psychology; war and nervous diseases; personalities and war; convulsions of mankind, and back to the land. A common thesis runs through all these statements, to wit: war is not a necessary expression of human nature and the world can and must be organized for peace. Such specific suggestions for the avoidance of war are included as (1) adequate food and shelter, (2) sufficient air and light per person, (3) a universal means of exchange, (4) room for expansion, (5) work programs suited to the capacity and aptitude of the individual, (6) the constructive use of leisure time and (7) educational programs developed to fit the needs of individual mental capacity for learning so that the best which is in the human being may be brought forth for the service of humanity. A Scotch physician gives advice about going back to the land:

> Only a return to its natural base in the land will now save civilization from destruction.

In the old classical legend, Hercules, god of Force when engaged in a wrestling match with the young giant Antaeus, was surprised to find he could not overthrow him. Finally he learned the secret—that his young opponent was gegenes, earth born, and that, so long as he kept one of his feet on the earth, strength was imparted to him against which no external power could prevail. So the Olympian lifted Antaeus clear of his Mother Earth and, there and then, crushed him to death in his arms.

Antaeus is civilization, and Hercules is the Machine, which is on the point of crushing it. Can we yet learn from this fable, or have things gone too far?

The importance of this pamphlet is in the fact that it is issued by a medical association. Its significance is enhanced by the appearance at about the same time of such books as William Alanson White: The Autobiography of a Purpose, and Karl A. Menninger's Man Against Himself, both of which propound the principle that the solution of human problems, including war, lies along a better realization and a wider application of the totality concepts in medicine, of which the psychosomatic movement in medicine is a further manifestation. Futile as one small group may seem in a world gone mad, it should be a source of pride and hope that the medical profession has set its face officially against war as it has in times past against other major threats to the safety and integrity of man.

Investigations on the Sterilization Efficacy of Gaseous Formaldehyde. By Gunnar Nordgren, Med. Lic. Acta pathologica et microbiologica Scandinavica, Supplementum XL. Paper. Pp. 165, with 11 illustrations. Copenhagen: Einar Munksgaard, 1939.

This monograph presents not only a thorough critical review of the subject but also the author's investigations in which improved and original methods were used, leading to conclusions of practical and theoretical value, based on thorough bacteriologic studies in which physical-chemical factors were well controlled and analyzed. The aim of the investigation is stated by the author to have been of "a practical nature: to be able to stipulate under what conditions formaldehyde sterilization is reliable." As test organisms many strains of non-spore forming and spore forming aerobic and anaerobic bacteria were used. These were placed on "test objects" of various materials and forms.

"According to generally accepted opinion the bactericidal effect of formaldehyde depends upon simple molecules while polymerized molecules, as such, are considered to be biologically inactive." The author questions the opinion that "dry" formaldehyde gas consists almost entirely of polymerized molecules at ordinary temperatures. As a result of his experiments he concludes: "Paraformaldehyde vaporizes at room temperature mainly in the form of simple formaldehyde. . . . Judging from experimental results it would seem that at least 90 per cent of the molecules are simple formaldehyde molecules. . . . Thus one should doubtless be able to abolish the prevailing theory that the oft indicated, inadequate effect of 'dry' formaldehyde sterilization is due to the polymerized state of the gas. To the extent that a reliable differentiation in bactericidal effect between 'dry' and 'moist' formaldehyde gas can be attained, other factors must be involved. . . . Paraformaldehyde evaporates even in vacuum very slowly. The tardy increase of the formaldehyde vapor pressure in a closed vessel containing paraformaldehyde would at least partly explain why 'dry' formaldehyde sterilization in practice often gives unsatisfactory results." Another source of failure may be the presence of water. It is stated that only 0.016 cc. of water is required to dissolve half the quantity of formaldehyde in 1 liter of air saturated with formaldehyde at about 18 C. "Slight moisture on, for instance, a more complicated instrument might probably therefore serve as an obstruction to the diffusion of the formaldehyde toward the inner infected parts of the instrument. For this reason it is imperative that one adopt a critical attitude toward the general method, in both disinfection and sterilization praxis, of seeking to saturate the moisture of the air by the evaporation of water in order to bring about condensation."

Briefly, the reviewer understands that the sterilization efficacy of formaldehyde is greatest in an atmosphere of water vapor saturated with formaldehyde gas but that instruments should not be wet when placed in the sterilizer and the condensation of water during the process of sterilization should be avoided. In the author's experiments gas pressure, vapor pressure, time of exposure and temperature were carefully controlled. Heat was found to enhance the bactericidal action of formaldehyde. Recovery of organisms after exposure to formaldehyde was more frequent after the use of a sulfite solution; ammonia was of little or no value as a neutralizing agent. "The bactericidal efficacy depends upon the relative moisture of the gas, in all probability through the effect it has on the dried condition of the bacteria (spores) themselves. Dry formaldehyde gas is

nevertheless able to kill even spores which are in a very dry condition. . . . The gas has at least as strong sporocidal effect on spores which are not dried up as would have a formalin solution with which the gas is in equilibrium. . . . Sixteen experiments comprise simple sterilization tests carried out with seventy strains" of spore forming and non-spore forming bacteria and molds. For these tests the "test objects" were pieces of glass on which the organisms had been smeared and allowed to dry at 37 C. for from fifteen to twenty minutes. "In all cases the test objects were found to be sterile within a shorter space than an hour under the effect of air which, at room temperature (20-22 C.), was from half to three quarters saturated with formaldehyde and approximately saturated with water vapor." Greater difficulties are encountered in the sterilization of coarse particles of soil, porous materials and instruments with canals such as catheters. "For a safe sterilization of ureteral catheters not even the 'formalin-vacuum principle' at 60° and an operation time of one hour is adequate. . . . Improvement is possible through previous evacuation followed by a relatively quick rise of pressure (by letting in air having a relative percentage of formaldehyde and water vapor as high as possible). . . . It must be pointed out that it is the rise of pressure as such, not the vacuum itself or the absence of air, which causes the penetration of the formaldehyde gas."

"The present prevailing opinion on formaldehyde sterilization must be completely changed. It should be unmistakably borne in mind that, although gaseous formaldehyde, as such, has a rather strong bactericidal efficacy, it has a very limited capacity to sterilize without the aid of specific technical expedients. Under such simple technical conditions as afforded by the Janet and Albarran principles, formaldehyde sterilizations can only be employed for very special purposes and with great precautionary measures. For more general purposes — for most of the objects which, in present day praxis, are treated in the Janet and Marion apparatuses — formaldehyde sterilization can only be made use of with the help of more complicated technical devices." The author describes the principles and uses of two such devices: (1) "a specific apparatus having no vacuum device, for the sterilization of one single instrument", such as an object "of simple shape, lacking canals or crevices, for instance, a simple endoscope"; (2) "an apparatus with a vacuum device for general purposes" in which alternate evacuation and admission of air saturated with formaldehyde may be employed.

A College Course in Hygiene. By K. Frances Scott, Ph.B., M.D., Associate Professor of Hygiene, Smith College, Northampton, Massachusetts. Boards. Price, $2.50. Pp. 202, with 48 illustrations by Dr. William Dunlop Sargent and Margaret J. Sanders. New York: Macmillan Company, 1939.

This is an excellent college manual evidently intended for use primarily in Smith College for Women. The approach is biologic. The first chapter deals with the biologic nature of the body. Subsequent chapters in part 1, which is devoted to hygiene as it concerns the individual, deal with the body's equipment for motion, equipment for energy production, the secretory function or chemical laboratory, the transportation systems (circulatory), metabolism and excretion, breathing, temperature control, equipment for acquiring information and equipment for coordination. The material is clearly, logically and briefly presented with numerous simple diagrams, charts, schematic drawings and silhouettes. The selection of material for practical usefulness has evidently been made with great care and excellent judgment. Elimination of extraneous material has contributed to the brevity of the work and yet is sufficiently complete to give the student an excellent orientation with relation to personal health. The second section is devoted to hygiene as it concerns the group, dealing with the human being's equipment for group living, his position as part of the race, and subsequent chapters taking up physical environment, control of the sources of supply, communicable diseases, special health needs and group agencies (public and private) for protecting health. Particularly complete, restrained and sensible are the sections relating to vitamins, stimulants, depressants, mental hygiene, sex and the venereal diseases. The venereal diseases are dealt with in connection with communicable diseases as is appropriate, and the sexual function is discussed in the chapters on the human being as part of the race immediately following the chapter on the human being's equipment for group living. The workbook section is commendably brief, consisting of knowledge tests and personal inventory on general health, nutrition, food habits, colds, sleep, periodic function and civic health knowledge, plus ventilation surveys and lighting surveys. There is a brief but adequate index. Brief reading suggestions follow each chapter. The most frequent reference given in these reading lists is to *Hygeia*, the Health Magazine. The book can be recommended without reservation for use in institutions where women are taught or as a study manual for adult groups of women anywhere.

Grundriss der Geschlechtskrankheiten. Von K. Zieler. Third edition by Dr. Georg Birnbaum, o. Professor und Direktor der Universitätsklinik und Poliklinik für Haut- und Geschlechtskrankheiten in Königsberg/Pr. Boards. Price, 4.90 marks. Pp. 213, with 19 illustrations. Leipzig: Georg Thieme, 1938.

This is the first revision of "Zielers Grundriss" in more than fifteen years. It is a brief discussion of the field of venereal diseases including gonorrhea, syphilis, soft chancre, venereal warts and nongonorrheal infections. This edition is by Birnbaum, a pupil of Zieler's. During the intervening years since the second edition political changes in Germany have definitely established the combating of venereal diseases as a public health problem. Therefore a brief discussion of the legal aspects of these diseases has been included. In the introduction, the point that prevention is more important than treatment is stressed. It is stated that there is little excuse for the continuance of venereal disease, it is so readily recognizable and treated. A third of the book is devoted to gonorrhea, including a brief discussion of the anatomy of the urethra, bacteriology, identification of the organism by staining and culture, the complications arising with treatment of each, explicit directions for examining both the male and the female, criteria for cure and a short discussion of the disease in children. Recent chemotherapeutic advances are not discussed, probably because the preparation of the book antedated them. Endocrine therapy in juvenile gonorrheal vaginitis is not discussed, nor is heat treatment. Complement fixation is regarded as merely a diagnostic adjunct. Vaccines are discussed at length. Soft chancre and venereal lymphogranuloma receive just a few pages; treatment of the latter with antimony and gold is briefly discussed. By far the greater part of the book is given to syphilis, including technic of preparation of the lesion for dark field examination, which the author believes is the most certain diagnostic point in recognizing syphilis. The lesions are thoroughly described and each drug is well discussed. Intramuscular mercury is favored by the author and the toxic effects are exhaustively shown. Malarial therapy is briefly discussed but no other forms of fever therapy are considered. In most respects the book fulfils the aim of the author. Many new trends in the field of venereal diseases are not included, probably because of the time element and the fact that the author intends to present briefly only facts that are certain.

Alcohol: Its Action on the Human Organism. By a Committee Originally Appointed by the Central Control Board (Liquor Traffic) and Later Reconstituted by the Medical Research Council. Third edition. Boards. Price, 30 cents; 1s. Pp. 176, with one illustration. New York: British Library of Information; London: His Majesty's Stationery Office, 1938.

In 1916 a distinguished British committee including such names as those of Cushny, Dale, Mott and Sherrington, later supplemented by Mellanby and Myers, prepared a statement on the effects of alcohol on the human body. In 1920 there was a careful revision, and a second edition appeared in 1924. The present edition has been prepared by a new committee, since some of the former members have died, and the book is now published on the authority of the Medical Research Council of Great Britain. It is an authoritative work as to the effects of alcohol on digestion and respiration and also considers its poisonous effects, its uses as a medicine, and the effect of alcohol on longevity. Here, it is the conclusion that mortality rates of persons especially exposed to the temptations of alcohol freely are unfavorable, but the statistical data now available do not suggest that a strictly moderate use of alcohol unfavorably affects the mortality rates of the users. The final conclusions are: "The temperate consumption of alcoholic liquors in accordance with these rules of practice may be considered to be physiologically harmless in the case of the large majority of normal adults; this conclusion, it may be added, is fully borne out by

the massive experience of mankind in wine-drinking and beer-drinking countries. On the other hand, it is certainly true that alcoholic beverages are in no way necessary for healthy life; that they are harmful or dangerous if the above mentioned precautions are not observed; further, that they may be definitely injurious for children and for most persons of unstable nervous system, notably for those who have had severe injuries of the head or who have suffered from attacks of mental disorder or from nervous shock."

Practical Dermatology and Syphilis. By Harry M. Robinson, M.D., Professor of Dermatology and Director of the Syphilis Clinic, University of Maryland School of Medicine, Baltimore. Cloth. Price, $4.50. Pp. 397, with 439 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1939.

Robinson presents a small textbook on dermatology which he states is "intended as an aid to the beginner in the study of dermatology (1) by helping him acquire a knowledge of the fundamentals of skin diseases, and (2) by showing how one may learn to recognize and diagnose the commoner diseases of this field." In his introduction he gives in a succinct manner a review of the "high spots" in dermatology with pertinent excerpts from some of the classic articles of the last decade. Since the work is intended as a small textbook on dermatology, the accounts are brief and there is no bibliography. There are forty-four pages on syphilis, and the subject on the whole is excellently treated. The illustrations are reproduced with a fair degree of accuracy. Figure 298, labeled Pemphigus foliaceus, shows a lesion in the left temporal area which impresses one as being more likely a patch of secondary vegetative dermatitis or epithelioma. The author deserves credit for knitting the details of his own diagnostic, clinical and therapeutic experiences into the text. While the book is an admirable small one and occupies a favorable position between the usual compend and the standard textbook on dermatology, it does not impress one as comparing with our better standard American textbooks.

Priests of Lucina: The Story of Obstetrics. By Palmer Findley, M.D., F.A.C.S. Cloth. Price, $5. Pp. 421, with 38 illustrations. Boston: Little, Brown & Company, 1939.

This book will be a welcome addition to the library of those members of the profession who are interested in medical history, whether or not they are obstetricians. It portrays the personalities of obstetricians, from the beginning of recorded literature to the present era, in a particularly interesting biographic style. The contents of the text are divided into two parts. Part one, comprising twenty-one chapters, presents in an especially readable way facts of obstetric history and biography. Part two deals with the history of special phases of obstetrics. Seldom does a book of this character present such a complete bibliography or one so well arranged for reference. To one interested in the history of medicine this is a treasure house of data. This alone should cause one to add the volume to one's library. The author states in the preface that he "has endeavored to select only the creative masters of the art, those who have contributed most largely to the making of an obstetric science, but it has not been possible to include all who have collaborated in the great work—it would be an endless task." He has selected well and made a decidedly valuable and interesting book.

Personality Changes After Operations on the Frontal Lobes: A Clinical Study of 32 Cases. By Gösta Rylander. Acta Psychiatrica et Neurologica, Supplementum XX. Paper. Price, 15s. Pp. 327, with illustrations. Copenhagen: Einar Munksgaard; London: Oxford University Press, 1939.

Any contribution on the functions of the frontal lobes of man is assured a large body of hopeful but apprehensive readers, for they have been disappointed often. Within this volume Gösta Rylander has gathered from the literature the salient opinions of other writers and has added a superb contribution of his own. The historical survey of twenty-seven pages covers the early epoch and the lessons learned from the study of brain injuries, tumors, Pick's disease, animal experimentation and partial excisions of the frontal lobes of man. The author's own contribution consists of follow-up examinations of thirty-two patients whose frontal lobes had been operated on from 1931 to 1938 in the Neurosurgical Clinic of the Serafimer Hospital. A critical selection of suitable cases, based on a study of the excellent hospital records, was made. The author not only examined the patients by appropriate psychologic tests, of which he gives an informative description, but also visited them in their homes. He laid particular emphasis on appraising their adaptation to their work and to society in general. The case reports, which cover 169 pages, are followed by a survey of the results of the investigation, a discussion and summary, an appendix of tables and a helpful bibliography of fifteen pages. The felicitous selection of Mrs. Helen Frey as translator has given to the members of the profession an English rendition of a decidedly meritorious work on the personality changes after operation on the frontal lobes of man.

The British Encyclopaedia of Medical Practice Including Medicine, Surgery, Obstetrics, Gynaecology and Other Special Subjects. Under the General Editorship of Sir Humphry Rolleston, Bt., G.C.V.O., K.C.B., M.D. Volume XI: Scarlet Fever to Testis, Undescended. Cloth. Price, $12. Pp. 676, with 94 illustrations. Toronto & London: Butterworth & Co., Ltd., 1939.

This volume is well up to the standard of the previous books in this system. The subjects discussed go from scarlet fever through such other main topics as sciatica, scurvy, sex hormones, sexual behavior and abnormalities, skin diseases, spinal cord diseases, spleen diseases, statistics, sterility, syphilis, and the testis. The authors are all British physicians of considerable note as investigators and practitioners in the fields of which they write. The volume is handsomely printed, profusely illustrated and well indexed.

A Textbook of Bacteriology: The Application of Bacteriology and Immunology to the Etiology, Diagnosis, Specific Therapy and Prevention of Infectious Diseases for Students and Practitioners of Medicine and Public Health. By Hans Zinsser, M.D., Consulting Bacteriologist to the Peter Bent Brigham Hospital and the Children's Hospital, Boston, and Stanhope Bayne-Jones, M.D., Professor of Bacteriology, and Dean, Yale University Medical School, New Haven, Connecticut. Eighth edition. Cloth. Price, $8. Pp. 990, with 116 illustrations. New York & London: D. Appleton-Century Company, Incorporated, 1939.

Although there have been rapid advances in bacteriology and immunology in the last few years which have necessitated the addition of a good deal of material, this edition is somewhat smaller than the preceding one. The section on pathogenic protozoa has been omitted, and redundant and obsolete material in other sections has been deleted. Together with minor changes, this has provided space for the addition of material based on recent systematic studies of genera and species, bacterial variability, bacterial metabolism, chemical progress in refining of antigens, viruses and bacterial chemotherapy. Parts of the book make heavy reading and in some respects it is more suitable as a reference book than as a textbook for beginning students of bacteriology. The book will be used doubtless for both purposes quite successfully.

Travaux pratiques et démonstrations de pharmacodynamie. Par L. Dautrebande, professeur de pharmacodynamie et de pharmacologie, Faculté de médecine, Université de Liége, E. Philippot, chef des travaux, F. Nogarède et R. Charlier. Paper. Price, 35 francs. Pp. 134, with 56 illustrations. Paris: Masson & Cie, 1938.

This laboratory manual on pharmacology is well organized and abundantly illustrated with kymographic tracings. In addition to the conventional pharmacologic experiments there is included material on such subjects as the carotid sinus and the technic of inducing gas anesthesia. The book goes briefly into the simpler chemical and biologic tests for poisons, and ten pages is devoted to methods for identifying war gases. On the whole, however, the book contains little that cannot be found in similar manuals published in this country. There is no index.

The Common Diseases of the Skin: A Handbook for Students and Medical Practitioners. By R. Cranston Low, M.D., F.R.C.P.E., F.R.S.E., Consulting Physician to the Skin Department, Royal Infirmary, Edinburgh. Third edition. Cloth. Price, 10s. 6d. Pp. 319, with 148 illustrations. Edinburgh & London: Oliver & Boyd, 1939.

This concise summary of present day dermatology gives the student and the practitioner an excellent introduction to the subject. The author's style is simple and easy to read, with emphasis on diagnosis and therapy of the commoner cutaneous disorders. In the chapters on eczema and urticaria the role of sensitization and focal infection is stressed. In the therapeutic sections most recent advances have been incorporated, although mention is not made of sulfanilamide and its possible uses in

dermatologic therapy or of the cutaneous reactions produced by it. In the chapter on drug eruptions mention should also have been made of phenolphthalein, phenobarbital and related compounds. The illustrations are well selected, including colored reproductions of moulages, black and white photographs, diagrams and characteristic histologic sections. Treatment in general is modern and not unnecessarily complicated. As an introduction to more complete volumes on dermatology, this book deserves unqualified approval.

A Classified List of Diagnoses for Hospital Morbidity Reporting. A Preliminary Report Based on a Study of 576,623 Hospital Discharges from 113 Hospitals in New York City in 1933. (WPA Project Number 665-97-3-54.) Welfare Council Publications 1939-IX. Paper. Price, 50 cents. Pp. 27. New York: Research Bureau, Welfare Council of New York City, 1939.

This is the first publication by the Welfare Council of New York City based on the results of the study of hospital discharges in New York City in 1933. The classified list of diagnoses of hospital morbidity reporting represents a study of nearly 600,000 discharges of patients from 113 hospitals in New York City. The diagnoses are based on the Standard Classified Nomenclature of Disease but for simplicity the diseases are listed under only 629 titles under such large divisions as "infectious diseases," "neoplasms," "neurology and psychiatric conditions" and "cardiovascular diseases." It will be most useful to some of the larger institutions and to those cities which desire to combine their morbidity figures from all different hospitals for extensive morbidity reports.

The Morphology of the Brachial Plexus with a Note on the Pectoral Muscle and Its Tendon Twist. By Wilfred Harris, M.D., F.R.C.P., Consulting Physician, St. Mary's Hospital, London. Cloth. Price, $8. Pp. 117, with 87 illustrations. New York & London: Oxford University Press, 1939.

This excellent monograph describes the investigation of the different forms of the brachial plexus found in 158 varieties of animals from the amphibia to man. It followed the author's desire in 1902 to trace the different components of the fifth cervical nerve in a monkey with a view to a possible nerve anastomosis operation on a young child with a localized poliomyelitic paralysis of the deltoid and spinatus muscles. There are included sections of amphibia, reptilia, aves and mammalia, the latter including thirty human plexuses. The illustrations show various brachial plexuses and attachments of shoulder muscles (especially the pectoralis major). Harris explains the cutaneous supply of the median and ulnar nerves on the back of the hand and the motor supply of the ulnar nerve to the dorsal interossei in man by finding the dorsal fibers joining the ventral branches of the inner cord and distributed with the median and ulnar nerves. This monograph is highly recommended to all neurosurgeons and neuro-anatomists.

Health Problems in Negro Colleges. Proceedings of the First Regional Conference for Health Workers in Negro Colleges, Atlanta, Georgia, April 7 and 8, 1939. Paper. Pp. 63. New York: National Tuberculosis Association, 1939.

This pamphlet represents the proceedings of the first Regional Conference for Health Workers in Negro Colleges. This conference was called in Atlanta, Ga., by the National Tuberculosis Association, the American Social Hygiene Association and the Atlanta School of Social Work. It deals with general administrative problems related to the health of Negro college students under four principal headings: the tuberculosis problem, venereal diseases, health examinations and the improvement of hygienic teaching in Negro colleges. It should be of interest to all persons concerned with the higher education and social welfare of the Negro.

The Evolution and Organization of the University Clinic. By Simon Flexner, M.D. Paper. Price, $1.25. Pp. 41. New York & London: Oxford University Press, 1939.

This little pamphlet combines two lectures given by Dr. Flexner at the Nuffield Institute in Oxford, England, in January 1938. The author traces briefly the development of the modern clinic and especially of the scientific laboratory, emphasizing the important features of organization of such modern institutions as the Rockefeller Institute.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Suspected Pregnancy or Ovarian Cyst; Failure to Use Friedman Test Negligence.—One of the plaintiffs, a married woman, consulted the physician defendant in either September or November 1934 relative to a possible pregnancy. The physician made a digital examination of the uterus. According to her testimony, he told her that she was pregnant. He testified, however, that he told her that she had an ovarian cyst, but she denied that he did so. Apparently she visited the physician's office from time to time thereafter and was examined, the physician defendant, according to the record, telling her repeatedly that she was pregnant. When she visited the physician in April 1935 her abdomen was distended and she complained that she had suffered severe pains during the previous month and had become very nervous. At that visit her husband asked her physician if there was not some way of determining whether his wife was or was not pregnant and her physician then suggested "the rabbit test," meaning thereby, presumably, the Friedman test or some similar test. The test was made and showed that the plaintiff was not pregnant. Thereafter an ovarian cyst about 6 inches (15.2 cm.) in diameter and weighing about 2 pounds (907 Gm.) was removed. The patient and her husband then sued the physician for malpractice. From a judgment in favor of the physician, the patient and her husband appealed to the Supreme Court of Washington.

In the course of the trial the plaintiffs offered to prove the number of "rabbit tests" that a chemist, the proprietor of a large local pathological and chemical laboratory, had made since 1931, the total number he made in 1934 and the number that he made for the defendant during that year. The trial court rejected the proffered evidence. The propriety of this rejection presented, according to the Supreme Court, the question to be determined on appeal.

It is well settled, said the court, that a physician must exercise that degree of care and skill which is ordinarily exercised by the members of his profession in the community in which he practices and in similar communities, having due regard for the state of medical and surgical science at the time. Ordinarily, whether a physician has exercised the degree of care and skill that the law requires is established by professional opinion, but this is not an invariable rule. There are instances in which facts alone prove negligence and it is unnecessary to have the opinion of persons skilled in a particular science to prove unskilled and negligent treatment. There is a difference, too, in malpractice cases, between mere errors of judgment and negligence in collecting beforehand data that are essential to the forming of a judgment. If a physician fails to inform himself as to facts and circumstances essential to the forming of a judgment and injury to the patient results from such failure, the physician is liable. Bearing these principles in mind, continued the court, we come to the question whether the chemist whose testimony was proffered should have been permitted to testify concerning the number of "rabbit tests" he had made.

The evidence showed that the "rabbit test" yielded correct results in 96 per cent of all cases. It was employed by physicians generally in the locality in which the defendant was practicing, in obscure cases. The physician defendant testified that the test was not in general use but was an aid and that he had from time to time employed it. Professional opinion was a unit in stating that where there was an ovarian cyst and the patient was not pregnant, it was correct practice to remove it, but that if the patient was pregnant it was correct practice to delay the operation, if it could be safely delayed, until after the birth of the child. An operation for the removal of the cyst while a patient was pregnant would in all probability result in the death of the child. In this case, the physician defendant testified that he suspected pregnancy and that he suspected also the presence of the cyst when he made the first examination of the plaintiff and that it was a matter of first importance when an ovarian

cyst was discovered to find out whether the patient was pregnant. The question then, continued the court, was whether the physician, in failing to employ the "rabbit test" earlier than he did and relying on the digital examination, neglected to collect data essential to a proper conclusion in the case. If he had discovered sooner that the patient was not pregnant, the cyst could have been removed earlier and the patient would have been saved from a long period of inconvenience and severe pain, resulting in a nervous condition.

The extent to which the "rabbit test" was applied in the locality in which the physician defendant practiced had a material bearing on the question of whether he was or was not negligent in not applying the test earlier. Courts have repeatedly held that the failure on the part of a physician to make a roentgenogram or to have a roentgenogram made as an aid to correct diagnosis, when x-ray machines are available and are commonly used by physicians in similar cases, may constitute actionable negligence. Applying the same principle to the utilization of the "rabbit test," it follows that the extent to which that test was utilized by physicians in the locality in which the physician defendant practiced was a material subject of inquiry in determining whether the physician was or was not guilty of negligence in failing to make use of the test at an earlier date. The testimony of the chemist which was proffered and rejected, said the court, was material and competent and its rejection was prejudicial error.

Judgment in favor of the physician defendant was reversed and a new trial ordered.—*Peterson v. Hunt (Wash.), 84 P. (2d) 999.*

Workmen's Compensation Acts: Back Injury; Objective Evidence of Injury—Determinative Effect of Lay Testimony.—The claimant, in the course of his employment, attempted to lift a bucket of nuts and bolts weighing about 60 pounds. He felt a sharp pain in the lower part of his back and in his hips and could not lift the bucket nor straighten up. An osteopath, whom the claimant's foreman advised him to consult, found, so he testified later, "a severe injury to the ligaments and muscles in the area of the back, in the location of the first lumbar vertebra." He believed that "a fracture or injury of the vertebra had occurred." A company physician ordered the disabled workman to a sanatorium, where he remained nine days. After he returned home he remained in bed for about three weeks more. Thereafter he instituted proceedings under the Louisiana workmen's compensation act for compensation for total and permanent disability. The trial court rejected his claim and he appealed to the court of appeal of Louisiana, second circuit.

The employer contended that there was no evidence of objective symptoms of the alleged injury and that the Louisiana workmen's compensation act made such symptoms a condition precedent to an award of compensation. The court believed, however, that the evidence adduced met the requirements of the statute. The court pointed out that there was evidence that the claimant complained of his injury immediately after the accident; that his foreman and his fellow employees saw that he was injured and assisted him to the osteopath's office; that the osteopath recognized the injury; that the employer's physician sent him to a sanatorium, and that certain patients in that sanatorium observed the claimant's distress and suffering during his stay there.

To substantiate the defendant's contention that at the time of the trial the claimant was not suffering from any disability, it relied principally on the testimony of six physicians. Some of them had made clinical examinations of the claimant and others testified solely on the basis of roentgenograms. Their testimony was in irreconcilable conflict with the testimony of four physicians called on behalf of the claimant. In any case, said the court, in which the medical testimony is as conflicting as here, the court is forced to look to the lay testimony for a solution.

It is immaterial, continued the court of appeal, whether or not a claimant can prove the exact injury he suffered. It is sufficient in this case for the claimant to show that his back was injured and the location of the injury and the fact that the injury renders him unable to perform ordinary manual labor. Were a workman required to prove the exact part of his back that was injured "he would be left to the mercy of the medical profession, which never fails to disagree as to the injury of a back." The lay testimony, however, in this case was overwhelmingly in the claimant's favor. It was shown beyond question that he had performed no manual labor since the accident and that on stated occasions he suffered pain and discomfort when he attempted to exert himself. The claimant, said the court, is either totally disabled to perform manual labor or he is an "A No. 1 malingerer." The record does not justify this court in finding him to be a malingerer. The court is, therefore, forced to find that he was totally disabled to perform work of a reasonable character at the time of the trial.

There is evidence in the record, said the court, that the claimant's back shows an arthritic condition. Practically all the medical witnesses testified that an injury to the back when in that condition will often cause a dormant arthritis to flare up and give trouble. Even if that is what happened, however, the injury is compensable.

The court accordingly entered a judgment in favor of the claimant.—*Phillips v. Yazoo & M. V. R. Co. (La.), 183 So. 43.*

Hospitals: Nonprofit Hospital Corporation Not Liable for Negligence.—The plaintiff was born in a hospital Oct. 6, 1926. He was placed in a crib in the nursery with several other infants, among them a premature baby. To afford warmth for the premature baby an incubator was improvised, using as a source of heat an electric light globe. Either because of the defective condition of the electric wiring by which the globe was put into service or because of the close proximity of the globe to the cotton bedding, the crib in which the premature baby was lying caught fire. That baby was burned to death and the fire passed from the crib in which it was lying to the crib in which the plaintiff was sleeping, and the plaintiff was injured. On behalf of the injured child, his mother sued the hospital for damages. The jury returned a verdict in favor of the plaintiff, but on motion of the defendant a judgment was rendered in its favor notwithstanding the verdict. From that judgment, the plaintiff appealed to the appellate court of Illinois, first district, third division.

There is no controversy, said the court, as to the happening or as to the cause or result of the injury sustained by the plaintiff. It was conceded, too, that if the defendant in the case was a charitable organization as defined by the laws of the state of Illinois it was not liable for the negligence of its servants and employees. The provisions of the charter, said the court, determine the character of the organization and the purposes for which it was organized. Where a corporation, as shown by the terms of its charter, is operated not for profit and has no provision for the issuance of stock or the payment of dividends to incorporators or stockholders and where it appears that its purpose is to conduct a hospital, the law recognizes it as a charitable institution. The evidence, the court thought, was sufficient to prove the charitable character of the hospital defendant in this case. The injuries were grievous and would enlist sympathy if that were one of the elements to be considered in arriving at a decision, but under the law the court was obliged to hold that no liability attached to the defendant hospital.

The judgment of the trial court was affirmed.—*Maretick v. South Chicago Community Hospital (Ill.), 17 N. E. (2d) 1012.*

Autopsies: Liability for Performance of Autopsy on Illegal Order of Justice of the Peace.—A workman, Love, instituted proceedings under the Texas workmen's compensation act for compensation for an injury allegedly due to his employment. Love died and a claim adjuster for the insurer of Love's employer procured from a justice of the peace an order for an autopsy. The autopsy was performed by the county health officer and another physician, each of whom was paid $50 by the insurance company. Information obtained through the autopsy was used by the insurance company to defeat the claim for compensation. Love's brothers and sisters sued the insurance company for having unlawfully procured the performance of the autopsy without their consent. The trial court directed a verdict in favor of the insurance company, but the court of civil appeals of Texas, Beaumont, reversed that judgment and remanded the case for a trial on its merits. *Love* v. *Aetna*

Casualty and Surety Company (Texas), 99 S. W. (2d) 646; abstr. J. A. M. A. **109**:387 (July 31) 1937. The insurance company then appealed to the Supreme Court of Texas.

In Texas, the Supreme Court pointed out, the authority of a justice of the peace to order an autopsy is derived exclusively from statute and may be lawfully exercised only for the detection of crime. It is to be presumed that a justice of the peace who orders an autopsy acts in the exercise of sound discretion and in good faith for the purpose of detecting crime, but this presumption is rebuttable. In the judgment of the Supreme Court, the testimony of the claim adjuster justified a finding that he had submitted the facts of Love's injury and death to the justice of the peace to induce that officer to order an autopsy for the purpose of determining whether or not Love had sustained a compensable injury and that the justice of the peace ordered the autopsy for that purpose. Such a finding by the jury would have destroyed the presumption of regularity of the justice of the peace's order for the autopsy and would have established that the justice of the peace ordered the autopsy for a purpose not authorized by law.

The Supreme Court of Texas therefore affirmed the judgment of the court of civil appeals, remanding the cause for a trial on its merits.—*Aetna Casualty & Surety Co. et al. v. Love et al. (Texas), 121 S. W. (2d) 986.*

Medical Practice Act (Utah): Revocation of License for Violating Narcotic Drug Act; Both Convicting Court and Licensing Agency Authorized to Revoke.—The medical practice act of Utah authorizes the Department of Registration to revoke or suspend the license of a physician guilty of unprofessional conduct, which the act defines to include, among other things, the prescribing of narcotic drugs in violation of law. The narcotic drug act of Utah, enacted subsequent to the enactment of the medical practice act, authorizes the court before which a physician has been convicted of violating its provisions not only to fine or imprison him but also, in its discretion, to revoke or suspend his license to practice.[1] Light, a licensed physician, was convicted of prescribing narcotic drugs in violation of the act, but the court did not revoke or suspend his license. The Department of Registration later instituted proceedings to effect that end. Light then petitioned the district court of Salt Lake County for a writ of prohibition to prevent further proceedings by the department. On demurrer, the trial court refused to issue such a writ and Light appealed to the Supreme Court of Utah.

The petitioner contended that the department had no jurisdiction to revoke or suspend the license of a physician convicted of violating the state narcotic drug act, since authority to revoke or suspend a license for such an offense was vested by the narcotic drug act itself exclusively in the court before which the physician was convicted. It is apparent, however, answered the court, that the state narcotic drug act intended to give the convicting court a power additional to that of fining and imprisoning a physician convicted of violating the act when it authorized it also to revoke or suspend his license to practice. If the court does not revoke or suspend the license, the Department of Registration, said the Supreme Court, still has the power to do so. This is shown by the fact that the clerk of the court, on conviction, is required by the act to send a copy of the judgment and sentence, together with the opinion of the court, if any, to the Department of Registration. If this sentence shows that the court has revoked or suspended a license, the department needs to go no further in that regard but has only the duty of seeing that the physician does not practice while his license is not in force. If the sentence does not include revocation or suspension, however, the department can proceed administratively to revoke or suspend the license of the convicted physician. Even independently of any criminal charge, too, the department may institute revocation proceedings. There is nothing inconsistent or incompatible in giving the court the power to revoke or suspend a license and at the same time leaving in the administrative board or department authority to proceed to the same end.

Accordingly, the Supreme Court affirmed the judgment of the court below, in effect permitting the Department of Registration to institute and maintain proceedings for the revocation or suspension of the license of the petitioner notwithstanding the fact that the court did not do so.—*Light v. Golding, Director of Department of Registration (Utah), 85 P. (2d) 114.*

1. In this respect the provisions of the Utah act correspond with those of the Uniform Narcotic Drug Act as formulated by the National Conference of Commissioners on Uniform Laws and enacted by many states.

Cosmetology: Electrolysis as "Beautifying the Human Face."—In New York City no person may conduct a beauty parlor without a permit from the board of health. The Sanitary Code defines a "beauty parlor" as a place "wherein the business of . . . beautifying the human . . . face, . . . or hands, is conducted for fee, charge, or hire." The defendant practiced electrolysis in a one story house located in a residential zone. She had applied for a permit to operate a beauty parlor but her application was denied because the building department would not certify to the propriety of a business use in a residence zone or district. She was convicted of operating a beauty parlor without a permit and appealed to the supreme court of New York, appellate division, second department.

The defendant did no manicuring or massaging but confined her activities to the removal of hairs, by electrolysis, from all parts of the bodies of patrons. There is no doubt, the court said, that the removal of unwanted hair from the human face is commonly deemed "beautifying the human . . . face," within the meaning of the Sanitary Code. The fact that the defendant removed hair from the body, not mentioned in the Sanitary Code, as well as from the face and hands, did not exclude her activity from the purview of the code. To interpret the provisions of the code so as to enable a person who does certain types of work, not mentioned therein, also, without a permit, to do work specifically within its terms, when the latter work is general and not casual or sporadic, would, the court said, be to nullify the statutory provisions and countenance clear evasion thereof. The removal of hair from the face was characterized, the court continued, as a "type of beauty culture" in a case holding that using electrolysis was not the unlawful practice of medicine. Likewise, it has been held that the use of electrolysis to prevent growth of hair is similar to the work of a barber in removing hairs on a man's face. *People* v. *Lehrman*, 251 App. Div. 451, 296 N. Y. S. 580, affirmed 276 N. Y. 479, 12 N. E. (2d) 166; abstr. J. A. M. A. **110**:839 (March 12) 1938.

In the opinion of the supreme court, the defendant conducted a beauty parlor without a permit in violation of the statute. The judgment of conviction was therefore affirmed.—*People v. Cohen (N. Y.), 8 N. Y. S. (2d) 70.*

Society Proceedings

COMING MEETINGS

American Academy of Pediatrics, Cincinnati, November 16-18. Dr. Clifford G. Grulee, 636 Church Street, Evanston, Ill., Secretary.

American Society of Anesthetists, Los Angeles, Dec. 14. Dr. Paul M. Wood, 745 Fifth Ave., New York, Secretary.

American Society of Tropical Medicine, Memphis, Tenn., Nov. 21-24. Dr. E. Harold Hinman, Wilson Dam, Ala., Secretary.

Pacific Coast Society of Obstetrics and Gynecology, Portland, Ore., Nov. 8-11. Dr. T. Floyd Bell, 400 29th St., Oakland, Calif., Secretary.

Radiological Society of North America, Atlanta, Ga., Dec. 11-15. Dr. Donald S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y., Secretary.

Society for the Study of Asthma and Allied Conditions, Philadelphia, Dec. 9. Dr. W. C. Spain, 116 East 53d St., New York, Secretary.

Society of American Bacteriologists, New Haven, Conn., Dec. 28-30. Dr. I. L. Baldwin, Agricultural Hall, University of Wisconsin, Madison, Wis., Secretary.

Southern Medical Association, Memphis, Tenn., Nov. 21-24. Mr. C. P. Loranz, Empire Bldg., Birmingham, Ala., Secretary.

Southern Surgical Association, Augusta, Ga., Dec. 5-7. Dr. E. Alton Ochsner, 1430 Tulane Ave., New Orleans, Secretary.

Southwestern Medical Association, El Paso, Texas, Nov. 9-11. Dr. M. P. Spearman, 1001 First National Bank Bldg., El Paso, Texas, Secretary.

Tri-States Medical Society of Texas, Louisiana and Arkansas, Marshall, Texas, Nov. 8-9. Dr. Robert K. Womack, Longview, Texas, Secretary.

Western Surgical Association, Los Angeles, Dec. 15-16. Dr. Albert H. Montgomery, 122 South Michigan Blvd., Chicago, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1929 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

9: 545-580 (Sept.) 1939

Preparation of Universally Compatible Ascitic Fluid for Transfusion. R. M. Choisser and Elizabeth M. Ramsey, Washington, D. C.—p. 545.

Silent, So-Called Primary Tuberculosis of Spleen. H. Fox, Philadelphia.—p. 549.

Effect of Ingested Sodium Chloride on Concentration of Hemoglobin. A. G. Sheftel, Los Angeles.—p. 554.

Leiomyofibromatosis: Multiple Tumors of Abdomen and Pelvis. W. M. German, Cincinnati.—p. 558.

Spindle Cell Sarcoma of Prostate. M. J. Fein, New York.—p. 564.

American J. Digestive Diseases, Huntington, Ind.

6: 429-504 (Sept.) 1939

Etiology, Diagnosis and Medical Management of Pancreatic Disease. E. H. Gaither, Baltimore.—p. 429.

Activity of Lower Part of Ileum of Dog in Relation to Ingestion of Food. D. M. Douglas and F. C. Mann, Rochester, Minn.—p. 434.

Over Two Thousand Estimations of Hydrogen Ion Concentration. M. A. Bridges and Marjorie R. Mattice, New York.—p. 440.

Phenolphthalein as Test for Gastrointestinal Ulceration in Experimental Animal. B. Slutzky and C. M. Wilhelmj, Omaha.—p. 449.

Anal Cryptitis. C. J. Drueck, Chicago.—p. 450.

Adenocarcinomatous Pedunculated Polyp of Esophagus: Report of Case. M. Feldman, Baltimore.—p. 453.

Abnormalities in Rectal Tone and Contraction in Paraplegia and Hemiplegia. S. J. Rosenberg and O. R. Langworthy, Baltimore.—p. 455.

*Nutritional Availability of Iron in Molasses. R. S. Harris, L. M. Mosher and J. W. M. Bunker, Cambridge, Mass.—p. 459.

New Approach to Prevention of Hemorrhages from Esophageal Varices as Occur in Cirrhosis and Banti's Disease. C. H. Drenckhahn, Urbana, Ill.—p. 462.

*Significance of Presence of Calcium Bilirubin Pigment and Cholesterol Crystals in Feces. F. Boerner, T. A. Johnson and M. Giannini, Philadelphia.—p. 466.

Physiologic Control of Normal Human Gastric Secretory Curve. C. M. Wilhelmj and A. Sachs, Omaha.—p. 467.

Available Nutritional Iron in Molasses.—Harris and his co-workers estimated the availability of iron in molasses by the chemical (dipyridyl) procedure and by the biologic assay procedure. The molasses used in their tests was prepared from Louisiana sugar cane. Juice is extracted by pressure from crushed cane, heated, treated with sulfur and lime to precipitate some of the impurities, clarified and concentrated to 40 degrees Baume by heating at 63 F. This sugar cane syrup is boiled down still further to crystallize the sugar, and the resulting liquor was called sample A. A portion of this "first" molasses is diluted with cane juice and reworked to obtain another extraction of sugar. The resulting liquor was called sample B. The "second" molasses is diluted with water, reboiled to obtain another extraction of sugar and the resulting liquor was called sample C. The "available" iron by the chemical method in the three kinds of molasses was found to be 97, 85 and 54 per cent, respectively. By the biologic (rat) method the availability was slightly more than 90, 80 and 50 per cent, respectively. The dipyridyl procedure is acceptable for the determination of the availability of iron in molasses. Molasses is a rich and inexpensive source of available iron. The authors point out that, although the iron in high grade molasses is more available than that in a lower grade of molasses, the higher grade is not as rich in total available iron. For example, 100 Gm. of molasses A furnished slightly more than 3.1 mg. of "available" iron, whereas the same quantity of molasses B contained approximately 5.1 mg. of "available" iron. The results obtained with molasses C do not agree with those of Shackleton and McCance, who reported that the iron in black treacle is 100 per cent available. In the authors' experience only 54 per cent was available. It is not correct to base one's judgment of a food on its total iron content, since iron availability varies with the kind of food. Molasses B is the type commonly used in the home; 85 per cent of its iron is available. Of the foods reputed to be excellent sources of iron, only liver compares favorably with molasses. Whipple and Robscheit-Robbins have listed chicken and beef liver, chicken gizzard, beef kidney, eggs, apricots and raisins as especially valuable in the treatment of anemia. From the authors' studies on these foods it appears that molasses is superior to all these foods in this respect and is, moreover, the most inexpensive food source of iron.

Significance of Bilirubin and Cholesterol in Feces.—The occasional presence of calcium bilirubinate, cholesterol or both in routine feces examinations led Boerner and his colleagues to examine 2,003 stools, in sixty-seven of which calcium bilirubinate, cholesterol crystals or both were found. In many instances the stools came from patients who were in the hospital for study of some condition unrelated to the biliary tract. Calcium bilirubinate alone was found in the feces in twenty-five cases and cholelithiasis was confirmed in eighteen. Of the remaining seven cases the diagnosis of cholelithiasis was not substantiated. Apart from cholelithiasis, two mechanisms may account for the presence of calcium bilirubin pigment in the bile and consequently in the feces: sudden release of noncalculous mechanical block of the main bile ducts or an increase in the serum bilirubin secondary to increased hemolysis may give rise to calcium bilirubinate in the bile in the absence of biliary disease. In a number of instances the first intimation of possible gallstone disease was the finding of calcium bilirubin pigment in the feces of a patient in whom that diagnosis was not suspected. Of fourteen cases in which cholesterol crystals alone were reported in the feces, there was only one in which the diagnosis of cholelithiasis was confirmed. Seven of the cases, however, were not studied for cholelithiasis.

American Journal of Medical Sciences, Philadelphia

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*Streptococcus Viridans Endocarditis Lenta: Clinicopathologic Analysis of Experience in Wisconsin General Hospital. W. S. Middleton and M. Burke, Madison, Wis.—p. 301.

Occurrence of Coronary Artery Thrombosis in Polycythemia Vera. H. R. Miller, New York.—p. 323.

Voluntary Hypercirculation. E. Ogden and N. W. Shock, Berkeley, Calif.—p. 329.

Brucellosis with Endocarditis: Report of Case with Failure of Sulfanilamide Therapy. K. M. Smith and A. C. Curtis, Ann Arbor, Mich.—p. 342.

*Effect of Sulfanilamide on Spermatogenesis in Man. N. J. Heckel and C. G. Hori, Chicago.—p. 347.

*Treatment of Pneumonia with Type Specific Immune Rabbit Serum. V. B. Callomon, Pittsburgh.—p. 349.

Respiratory Defense Mechanism: Its Relationship to Pulmonary Diseases. I. L. Applebaum, Newark, N. J.—p. 356.

*Studies on Oxyuriasis: XVIII. Symptomatology of Oxyuriasis as Based on Physical Examinations and Case Histories on 200 Patients. F. J. Brady and W. H. Wright, Washington, D. C.—p. 367.

Platelets in Pernicious Anemia, with Review of Literature. F. K. Paddock and Katharine Edsall Smith, New York.—p. 372.

Erythroblastic Anemia: Report of Two Cases in Adult Siblings, with Review of Theories as to Its Transmission. Dorothy W. Atkinson, San Francisco.—p. 376.

Mitotic Leukoblasts in Peripheral Blood in Infectious Mononucleosis. H. Bowcock, Atlanta, Ga.—p. 384.

Prognostic Significance of Eosinophils in Blood in Pneumonia. M. M. Bracken, Pittsburgh.—p. 386.

Evaluation of Phenolphthalein Test of Woldman. R. Le Vine and J. B. Kirsner, Chicago.—p. 389.

"Numeral Test" in Transverse Lesions of Spinal Cord. R. Wartenberg, San Francisco.—p. 393.

Effect of Alterations in Metabolic Rate on Action of Insulin. G. W. Hayward and G. G. Duncan, Philadelphia.—p. 396.

Cevitamic Acid Deficiency: Frequency in Group of 100 Unselected Patients. J. D. Croft and L. D. Snorf, Evanston, Ill.—p. 403.

Streptococcus Viridans Endocarditis Lenta.—Middleton and Burke present the clinical and pathologic features of eighty-eight cases of Streptococcus viridans endocarditis lenta which were observed at the Wisconsin General Hospital. They think that some of the details of the clinicopathologic analysis merit special emphasis. They adduce further evidence in support of a close relationship between congenital and rheumatic lesions of the heart and endocarditis lenta. Acute upper respiratory infections, rheumatic fever, infected abortion, dental extraction and massage for nonspecific prostatitis apparently served as precipitating factors in the development of certain cases of this condition. Contrary to the accepted opinion, congestive heart failure may attend or mask this condition. The clinical manifestations and course are varied and inconstant. After the

cardiac changes, particular attention was directed to its toxic and its embolic features. Splenic and renal changes, including embolism, were frequent. Mycotic aneurysms offered serious diagnostic problems. Cerebral accidents were not infrequent. Occasionally a mycotic aneurysm of a cerebral vessel may explain certain neurologic phenomena of this condition. Again the clinical picture may suggest thyrotoxicosis, and the unexplained elevation of the basal metabolic rate may add to the diagnostic confusion. This study offers material support to the importance of the diagnostic triad petechiae, splenomegaly and a positive blood culture for the Streptococcus viridans. Given the background of a congenital or a rheumatic heart lesion and a remittent fever, this triad offers the logical direction of attack. The prognosis of Streptococcus viridans endocarditis lenta is grave. Only inferential evidence of the pace of the decline is offered by the circulatory, renal, embolic, toxic, constitutional and hematologic reactions. Although remissions of varying durations and degrees are the rule, certain of these patients undergo a rapidly progressive decline. Attention is directed to the ominous significance of the euphoria that attends late remissions. This group included one instance of healed endocarditis lenta. The clinical activity apparently occurred at a period previous to the hospitalization. In the remaining eighty-seven cases all treatment was unavailing.

Effect of Sulfanilamide on Spermatogenesis.—Heckel and Hori say that the administration of sulfanilamide derivatives to man has been thought to influence spermatogenesis. To study this problem the authors analyzed the semen of eleven patients before and after sulfanilamide was given. They describe their method of examination and in a table they show the number of specimens examined, the total number of spermatozoa and the percentage alive before, during and after treatment; the time specimens were obtained in relation to the treatment and the duration of the treatment. The sulfanilamide was given by mouth up to a total of 40 grains (2.6 Gm.) daily, except when the drug was not tolerated, and then the dose was reduced or the patient was put on a rest period for two or three days. In contrast to other reports, these data indicate that in eleven cases there were no noteworthy effects on the total number or percentage of live spermatozoa from the use of sulfanilamide. Such variations as occurred in the spermatozoa counts during and after treatment were no greater than the variations which occurred before the drug was given.

Type Specific Immune Rabbit Serum in Pneumonia.—Callomon reports experiences with type specific antipneumococcus rabbit serum in forty-five cases. Included in this series are cases of pneumonia of types I, II, IV, V, VII and VIII. The only factor entering into their selection was the availability of a homologous immune serum at the time of their admission. In the majority of cases the product employed was unconcentrated. In a few of the more recent cases a concentrated preparation was administered. All cases reported showed roentgenographic evidence of consolidation and a positive blood culture or sputum in which the pneumococcus was the predominating organism. A history, physical examination, urine analysis, blood count, blood culture, sputum examination and roentgenogram of the chest were obtained on admission. Blood cultures were taken at two day intervals or more frequently when indicated. Identification of the type of pneumococcus present in the sputum was made by the Neufeld method and in many cases confirmed by passage through the mouse. Before treatment was instituted, all patients were given ophthalmic and intracutaneous tests for sensitivity to the specific serum which was to be used. The usual precautions, advisable in all serotherapy, were observed. When a positive intracutaneous test was associated with a negative ophthalmic test, the administration of serum was undertaken, but with more than the usual caution. All serum was given intravenously. At first, doses of 20,000 units were given at two hour intervals. Later this plan of treatment was altered, as the administration of larger doses seemed preferable in order to introduce the total dose in as short a time as possible. Following an initial dose of 20,000 units, one or more doses of 100,000 units were given until it was apparent that the disease was being brought under control. Subsequently, smaller doses were given as seemed indicated until recovery was complete. In several cases one injection of 100,000 units following the initial dose of 20,000 units was sufficient to secure the desired result. Supplementary treatment consisted only of dietary regulation and symptomatic treatment, including oxygen administration, when indicated. Regarding the results obtained with this treatment, the author says that two deaths occurred in this series. Premature recovery by crisis or rapid lysis ensued in thirty-six cases. No serious serum reactions were observed.

Symptomatology of Oxyuriasis.—Brady and Wright made studies in 200 cases of oxyuriasis. This material included persons seeking treatment for known pinworm infestation, persons referred to them because of symptoms suggestive of oxyuriasis, and persons in whom pinworms were detected by anal swab examinations made in the course of studies on the incidence of oxyuriasis. Comparative studies were made on two control groups. One group of seventy-two persons was negative for pinworms on examination by the swab method, but they lived in households together with infested subjects. A second group of twenty-one persons was negative for pinworm and lived in homes in which no member of the family was found infested. In each of the 200 cases of oxyuriasis the history was taken, a physical examination was made, a stool sample was examined for helminth ova, anal swabs were made, and in girls a vulvar swab was made. The opinion is expressed that symptoms may be caused by mechanical stimulation and irritation by the parasite, by allergic reactions, and by the transportation of organisms to places where they may become pathogenic. Many infested children showed gains in weight, improvement in color, and disappearance of dark circles under the eyes after treatment. There was an average eosinophil percentage of 5.1 in 144 pinworm cases compared to 3.7 in twenty-one children coming from households in which all persons were free from pinworms. There is too much deviation from the mean for these figures to assume statistical significance, but it is likely that there is a slight increase in eosinophil percentage in oxyuriasis. One case presented symptoms of nausea and vomiting that could not be attributed to causes other than the pinworm infestation. These symptoms disappeared when the pinworm infestation was eradicated. The authors found no proof that abdominal pain and oxyuriasis were directly related. Only one patient of the 200 had had an appendectomy. The appetite in many cases was much improved after treatment. It is believed that pinworms cause conscious sensation when moving on the rectal and anal mucosa but that no sensation is felt in the majority of cases after the pinworm has migrated onto the skin. Allergic reactions to pinworm products are probably associated with the marked sensation experienced by some few persons from skin migrations. Enuresis was not found to be more common in infested patients than in noninfested controls. Evidence is presented that a pinworm vaginitis may be much more frequent than it has been considered to be in the past. Restlessness and insomnia are symptoms occurring in pinworm cases. Restlessness in school may lead to scholastic difficulties. The feeling of shame that an impressionable child may have from the consciousness of having pinworms may have repercussions in the behavior of the child. Evidence to show that pinworms cause nervous irritability was inconclusive.

American Journal of Ophthalmology, St. Louis

22: 953-1070 (Sept.) 1939

So-Called Oguchi's Disease in the U. S. A.: Case. Bertha A. Klien, Chicago.—p. 953.
Practical Use of Homatropine-Benzedrine Cycloplegia: Further Report. L. S. Powell, Lawrence, Kan.—p. 956.
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Isolated Rheumatic Nodule of Upper Eyelid: Report of Two Cases. J. S. Guyton and J. M. McLean, Baltimore.—p. 985.
The Need for Social Service Work in Glaucoma. A. F. Jensen, Grand Forks, N. D., and H. S. Gradle, Chicago.—p. 993.
Ophthalmomyiasis Interna Anterior: Report of Hypoderma Larva in Anterior Chamber. C. S. O'Brien and J. H. Allen, Iowa City.—p. 996.
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Prophylactic Foreign Protein Therapy in Cataract Extraction. C. A. Noe, Cedar Rapids, Iowa.—p. 1014.

American Journal of Surgery, New York

45: 417-614 (Sept.) 1939. Partial Index

Tumefactions of Abdominal Wall. W. H. Meade and W. R. Brewster, New Orleans.—p. 419.
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Pigmented Nevi, with Special Reference to Their Surgical Treatment. J. W. Maliniac, New York.—p. 507.
*Impurities in Ether. H. H. Bradshaw, Philadelphia.—p. 511.
*Appendicitis Complicated by General Peritonitis: Method of Treatment That Lowers Mortality Rate. E. G. Williamson, and L. M. Rankin, Philadelphia.—p. 528.
Treatment and Management of Burn Cases. H. J. Lavender, Cincinnati.—p. 534.
Treatment of Burns. H. D. Cogswell, Tucson, Ariz., and C. Shirley, Tyler, Texas.—p. 539.
Traumatic Torsion of Ovarian Pedicle: Medicolegal Study with Presentation of Cases and Review of Literature. H. Sneierson, Binghamton, N. Y.; J. Schlesinger, College Point, N. Y., and A. E. Gold, Binghamton, N. Y.—p. 546.

Impurities in Ether.—Bradshaw reports a case in which death in convulsions occurred during the administration of nitrous oxide-oxygen-ether. Some blood was obtained for examination before death. The blood showed an oxygen content of 6.9, oxygen capacity of 14.6, saturation of 47.3 and a carbon dioxide content of 61 volumes per cent. The concentration of sugar was 400 mg. per hundred cubic centimeters of blood (intravenous dextrose was being administered). The ether was analyzed and showed aldehyde present, 1 : 50,000 in two samples. No other impurities were found. Although 100 per cent oxygen was given for a period of ten minutes the cyanosis became greater and the convulsions continued. The oxygen content and capacity of the venous blood were low, with a low saturation. The carbon dioxide content was within normal limits. Excess carbon dioxide, hypoglycemia and lack of preoperative medication have been mentioned as causes of these convulsions. However, none of these conditions could have been active in this case. The only positive observation was a low oxygen content of the venous blood despite the administration of 100 per cent oxygen.

Appendicitis Complicated by General Peritonitis.—Williamson and Rankin treated thirty-two cases of appendicitis complicated by general peritonitis without a fatality. They attribute this result to the immediate removal of the appendix, after a reasonably brief period of preoperative preparation. Rapid evacuation of the septic material was secured by placing the patient in the ventral position. This rapid elimination of irritating material also tends to prevent postoperative adhesions and related postoperative complications. They prevented sepsis in the abdominal wound by leaving the wound open. Anaerobic bacteria cannot grow in air. If this factor were taken into consideration in the treatment of general peritonitis complicating appendicitis, it is doubtful that there would be need for bacterins, serobacterins, vaccines and the like against anaerobic bacteria. Thus the open wound prevents sepsis in abdominal wounds. Paralytic ileus is treated mainly by prevention. The ventral position aids considerably. The efficacy of prostigmine for this purpose has been demonstrated. This drug maintains the muscular tone of the intestine by preventing parasympathetic paralysis. In large doses it is a parasympathetic stimulant. In short, the peritoneum was closed down to the drains, the fascia and skin were left open and the wound was packed with gauze saturated with tincture of merthiolate, azochloramide or similar antiseptic. Deep through and through retention sutures were put in but left loose in order to pull the edges of the wound together gradually as the infection disappeared. When the patient was returned from the operating room he was immediately put on his abdomen and the head of the bed was elevated from 8 to 12 inches. Routine treatment consisted in hypodermoclysis of saline and dextrose solution and saline solution intravenously. An ampule of prostigmine was given every four hours and morphine was used for pain. Contrary to expectations the patients complained of little discomfort because of the position. The dressings were quickly saturated with the drainage from the abdomen, necessitating frequent changing during the first twenty-four hours. The amount of discharge by far exceeded that of patients placed in the Fowler or other positions. This, because of rapid elimination of toxic material, undoubtedly accounted for the rapid drop in the temperature and pulse rate. As soon as they were tolerated, water and then liquids were given by mouth; after thirty-six to forty-eight hours the patient was put on his back. All patients were discharged from the hospital well after an average stay of 20.9 days and the wounds were healed, with the exception in a few cases of a small area at the site of the drains.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

23: 549-684 (Sept.) 1939

Some Problems in Control of Syphilis as a Disease. J. H. Stokes, Philadelphia.—p. 549.
*Treatment of Postarsphenamine Jaundice. L. J. Soffer, New York.—p. 577.
Malarial Treatment of General Paresis: Relation of Height, Duration and Frequency of Fever to Clinical and Serologic Results. I. Kopp and H. C. Solomon, Boston.—p. 585.
Sulfanilamide versus Sulfanilyl Sulfanilamide in Gonococcic Infections. B. J. Walzak, Cleveland.—p. 597.
*Sulfanilamide in Chancroid Disease. R. B. Greenblatt and E. S. Sanderson, Augusta, Ga.—p. 605.
Death Following Mapharsen Therapy: Report of Case. S. D. Simon and A. Iglauer, Cincinnati.—p. 612.
Clinical Application of Twenty-Minute Staining Method for Spirochaeta Pallida in Tissue Sections. A. A. Krajian, Los Angeles.—p. 617.
Simplified Technic for Administering Old Arsphenamine: Report on 16,943 Injections Given at Vanderbilt Clinic. A. B. Cannon, New York.—p. 621.

Postarsphenamine Jaundice.—Since hepatitis is difficult to reproduce experimentally, its clinical treatment is based on empirical experience and therefore Soffer points out that the prevention and treatment of postarsphenamine jaundice assume increasing importance. When it is considered that from 5 to 10 per cent of the general adult population has syphilis, that a considerable number of this group is receiving antisyphilitic treatment and that in 1 per cent of this treated group jaundice will develop with a mortality rate varying from 1 to 6 per cent, there is reason for concern as to the proper methods of treatment. From a review of the clinical and experimental data presented in the literature concerning the treatment of arsphenamine jaundice it is seen that a high carbohydrate diet is well accepted as an important therapeutic measure. Such diets should consist of from 400 to 600 Gm. of carbohydrates daily. This should be divided into five or six feedings. As the sugars fructose and dextrose are most readily converted into glycogen by the liver, foods made up of these carbohydrates should be used. Thus the most desirable are cane sugar, which is hydrolyzed into dextrose; honey, which is mostly dextrose and fructose; and fruit juices. When the amount of carbohydrate taken orally is inadequate, diets should be supplemented by a constant intravenous drip of a 5 per cent solution of dextrose. Insulin is indicated only when glycosuria is present. The use of cholagogues and choleretics in the treatment of arsphenamine jaundice is unsound.

Sulfanilamide for Chancroid.—Greenblatt and Sanderson have used sulfanilamide in the treatment of thirty-three cases of chancroid disease. The doses varied in individual cases, the average being from 400 to 500 grains (26 to 32.5 Gm.) of sulfanilamide. The by-effects were nausea, anorexia, dizziness and cyanosis. The twenty-seven ambulatory patients were usually given from twenty-five to forty tablets of sulfanilamide at a time with instructions for medication and to return every few days. Treatment was discontinued in one case because a rash developed, in two because of excessive vomiting and in one because of cyanosis. With cessation of treatment the untoward effects abated. Dizziness was the most frequent complaint, but treatment was never discontinued because of it. Surgical procedures other than aspiration of buboes were not performed. The therapeutic results, for the greater part, were so consistently good that the drug is regarded as a specific. The previously reported results of the British and American investigators are substantiated. Sulfanilamide proved more efficient than any of the standard methods in vogue. It succeeded in some cases in which vaccine therapy had failed.

Archives of Dermatology and Syphilology, Chicago

40: 521-686 (Oct.) 1939

*Immunotherapy for Coccidioidal Granuloma: Report of Cases. H. P. Jacobson, Los Angeles.—p. 521.
Pyoderma Gangraenosum, Onychogryphosis and Onycholysis with Ulcerative Colitis. Ida J. Mintzer, Jamaica, N. Y.—p. 541.
Diseases of Skin in Oklahoma Indians. H. Fox, New York.—p. 544.
Differential Diagnosis of Keratosis Blennorrhagica and Psoriasis Arthropathica. E. Epstein, Oakland, Calif.—p. 547.
Dermatitis Nodularis Necrotica: Report of Case in Which Changes Characteristic of Lymphosarcoma Were Observed at Necropsy. H. A. Nieman, Dayton, Ohio, and F. Wise, New York.—p. 560.
Active Spectral Range for Phytogenic Photodermatosis Produced by Pastinaca Sativa (Dermatitis Bullosa Striata Pratensis, Oppenheim). T. Jensen and K. G. Hansen, Copenhagen, Denmark.—p. 566.
Dermatofibrosarcoma Protuberans: Report of Six Cases. G. W. Binkley, Cleveland.—p. 578.
*Abscesses of Sweat Glands in Adults. P. Tachau, Chicago.—p. 595.

Coccidioidal Granuloma.—Theoretically, the ideal treatment of infectious diseases seems to be the administration of immunogenic antigens capable of activating the tissues and fluids to production of immune bodies. With this thought in mind, Jacobson decided to give vaccine treatment a trial in the management of coccidioidal disease. Since 1936 he has treated twenty-four cases of coccidioidal infection in its various clinical manifestations by this method. The character, extent of involvement and clinical course of the infection varied considerably. For the most part the clinical picture at the commencement of treatment was of the subacute variety. Evidence of past or present pulmonary involvement was present in the majority of cases. Next in frequency was involvement of the cutaneous-subcutaneous system, either as a primary manifestation or secondary to pulmonary or other systemic or structural coccidioidal disease. Involvement of bone was present in about 30 per cent of the cases. The aim of all therapeutic efforts was the raising of the patients' level of resistance to the existing infection. Accordingly, all febrile patients were kept in bed at complete rest. Nutritious and adequate diet, sunshine and fresh air played a definite part in the therapeutic regimen. Halibut liver oil with viosterol was given to all patients, and those seriously ill received injections of ascorbic acid daily or on alternate days. Anemic, dehydrated and undernourished patients also received blood transfusions, infusions of dextrose and parenteral injections of liver extract, according to clinical indications. Injections of vaccine constituted the specific part of the treatment. The vaccine was at first given subcutaneously, but later it was administered by the intravenous route. The standard initial dose has been 0.05 cc., and each succeeding injection has been increased by 0.05 cc. at intervals of from eight to fourteen days. In instances of unduly severe constitutional reaction, the dose of the succeeding injection was not increased and the interval was lengthened. A course consisted of from twelve to fifteen injections. Most patients received two or more courses of injections, punctuated by intervals of rest of from six to eight weeks. Five of the patients are still under treatment. Three are ambulatory and engaged productively but come to the office for injections of vaccine at regular intervals. All others have been discharged as fully recovered or are reporting regularly for observation. Two patients, one with widespread meningeal involvement and another suffering from the acute fulminating type of the disease, died. Specific immunogenic therapy is a rational procedure theoretically and has proved its worth clinically.

Abscesses of Sweat Glands.—Tachau reports 107 cases of sweat gland abscesses of the axilla. In 26 per cent a symmetrical involvement of both axillas was noted. In the others only the right or the left axilla was infected. In ten cases the abscess formation must be considered as a complication of local or generalized inflammatory dermatoses (contact dermatitis, eczema, epidermophytosis, erythrasma or arsphenamine dermatitis). Two patients were observed with abscesses of the sweat glands secondary to scabies and furunculosis, and another with Bockhart's folliculitis. One patient had retrograde lymphangitis extending down the arm. In other regions the author never observed a coincidental or successive involvement of many apocrine glands. Thus, only single abscesses running an acute course were occasionally observed around the nipple, on the pubic area, on the labia majora and around the anus. The infection of the apocrine glands starts from the outside. Local inflammatory processes, irritation by depilatories or shaving or the friction of tight clothing often favors the infection. They should never be considered as the actual causes. According to present knowledge, abscesses of the sweat glands are due to infection with Staphylococcus pyogenes aureus (and perhaps albus or citreus). The cultivation of streptococci or other germs from the abscesses does not prove their etiologic significance. The prognosis of abscesses of the apocrine glands is always favorable. The treatment of a single abscess consists in local application of dressings with a mild ointment (3 per cent of boric acid in petrolatum) or topovaccines, such as Sherman's mixed antivirus cream. Wet applications are not advisable, since they favor maceration and may give rise to the formation of new abscesses. As soon as softening occurs, a small incision is made for evacuating the pus. This is followed instantly by a quick and complete cure. Even in the axilla this simple treatment succeeds in uncomplicated cases. When the abscesses multiply and the patient is disabled, treatment with roentgen rays is the method of choice. In many cases a small dose suffices to give relief (from 100 to 120 roentgens, 70 to 80 kilovolts, filtered by 3 mm. aluminum; focal skin distance, from 25 to 30 cm.; diameter, from 10 to 15 cm.). Two or three days later the pain is usually gone. For more resistant lesions this dose must be repeated once or twice at intervals of ten days. Of thirty-seven patients treated since 1931 according to this technic, eight were cured after only one dose of from 100 to 120 roentgens; ten were cured after two exposures, or from 200 to 240 roentgens, while seventeen needed three exposures, or from 300 to 360 roentgens. In only two cases did considerable residual infiltrations or sinuses make it necessary to repeat the x-ray cycle after an interval of six or more weeks. Recurrences were never seen in this series.

Arkansas Medical Society Journal, Fort Smith

36: 87-102 (Sept.) 1939

Relationship Between Heart Disease and Chronic Pulmonary Affections. C. T. Chamberlain, Fort Smith.—p. 87.
Present Status of Antipneumococcus Serum and Sulfapyridine in "Management of Pneumonias." F. E. Schmidt, Chicago.—p. 91.
Electrocardiography. S. A. Thompson, Camden.—p. 93.

Connecticut State Medical Society Journal, Hartford

3: 479-540 (Sept.) 1939

Treatment of Burns. R. D. McClure, Detroit.—p. 479.
Treatment of Wounds. A. H. Bissell, Stamford.—p. 484.
Factor of Delay in Recognition of Common Surgical Conditions. E. Ottenheimer, Willimantic.—p. 487.
Problem of Clett Lip and Cleft Palate. C. C. Kelly, Hartford.—p. 490.
Urogenital Deformities. C. H. Neuswanger, Waterbury.—p. 492.
Congenital Orthopedic Deformities. A. S. Griswold, Bridgeport.—p. 494.
Management of Congenital Defects of Nervous System. W. J. German, New Haven.—p. 498.
Medical Air Raid Preparations in England. C. W. Goff, Hartford.—p. 504.

Johns Hopkins Hospital Bulletin, Baltimore

65: 223-290 (Sept.) 1939

Actions of Procaine on Neuromuscular Transmission. A. M. Harvey, London, England.—p. 223.
*Squamous Metaplasia, Simulating Carcinoma, Associated with Prostatic Infarction. O. S. Culp, Baltimore.—p. 239.
Chemical Reactions of Nicotinic Acid Amide in Vivo. E. G. Ball, Baltimore.—p. 253.
Relation of Psychiatry to Internal Medicine. T. A. C. Rennie, Baltimore.—p. 265.
Use of Low Temperature Ball Mill for Preparation of Pollen Extracts. H. Eagle, C. Arbesman and W. L. Winkenwerder, Baltimore.—p. 283.

Squamous Metaplasia and Prostatic Infarction.—Squamous cell metaplasia and infarcts of the prostate have been described independently by several authors but Culp believes that the frequent coexistence of these two pathologic processes has been overlooked. In a recent routine study of a prostate removed by operation, islands of squamous epithelium were observed along the margins of three infarcts. The provisional diagnosis was early squamous cell carcinoma. Further study of the remainder of the prostate showed only typical glandular hyperplasia. Eight additional prostatic infarcts, occurring in seven different cases, were studied and in each instance similar histologic changes were seen, limited to the periphery of the infarcted areas. The uniformity of these observations indicates that benign metaplasia frequently is associated with prostatic infarction and may be misinterpreted as carcinoma.

Journal of the Mount Sinai Hospital, New York

6: 113-168 (Sept.-Oct.) 1939

Function of Thymonucleic Acid in Living Cells. E. Hammarsten, Stockholm, Sweden.—p. 115.
Psychic Factors in Recurrent Graves' Disease. S. S. Bernstein, New York.—p. 126.
Roentgenkymography in Diagnosis of Myocardial Infarct, with Normal Electrocardiograms. M. L. Sussman, New York.—p. 130.
*Angina Pectoris of Psychogenic Origin. A. M. Master, S. Dack and H. L. Jaffe, New York.—p. 134.
Deficiency Syndrome and Diffuse Inflammation of Central and Peripheral Nervous System. J. Marmor, New York.—p. 138.
A Chemist Looks at Surfaces. H. Sobotka, New York.—p. 141.
Experimental Anticancerous Immunity. L. Gross, Paris, France.—p. 146.

Angina Pectoris of Psychogenic Origin.—Master and his associates point out that generally the anginal syndrome is caused by coronary artery disease and can be differentiated from a functional syndrome by the type of pain. In the organic type the pain is nearly always substernal and occurs as a rule after exertion, meals or excitement, whereas in the functional type the pain is usually over the precordium or nipple, often lasts longer and is not related to effort. In the main, this differentiation holds true but that angina of psychogenic origin may also be substernal and come on with exertion is illustrated by the case that they report. Although the anginal syndrome for which the patient (29 years of age) presented himself was characteristic of coronary artery disease and at one time was actually diagnosed coronary occlusion by a cardiologist, after four years it became obvious that it was merely the first symptom in what later became a well established neurotic complex. There certainly was no organic heart disease, for, after four years, the physical examination and all laboratory tests are normal. The authors are cognizant of the claim of some authors that angina pectoris due to coronary artery disease may be present in the absence of confirmatory evidence of any kind. However, they believe that this is rare if all tests are considered, particularly after a period of several years of observation. While the physical examination of the heart, fluoroscopy, electrocardiogram, exercise tolerance, and vital capacity may individually remain normal, it is improbable that all of these will do so. In the mechanism of pain in coronary artery disease a nervous mechanism is important, as even when organic coronary artery disease is present the frequency and severity of the anginal syndrome are greatly influenced by mental and emotional factors or, in the words of Heberden, "by passionate affections of the mind." Two patients with similar degrees of coronary artery disease may suffer pain of different severity, depending on the psychic makeup of each patient. Psychiatrists have emphasized the importance of the heart as the "specific sense organ of anxiety" and the close interrelation of the brain with the innervation of the heart. And, indeed, precordial pain is often the major symptom of a neurosis without organic basis. While the pain of organic heart disease is usually related to effort, not infrequently such an association is lacking. And pain of psychogenic origin may come on with effort occasionally. Exertion produces changes in pulse rate and contraction of the heart which in susceptible persons may cause sensations of pain, as was true of the patient presented. It is thus sometimes impossible to differentiate an anginal syndrome of organic origin from a functional one by the type of pain and its relation to effort.

Journal of Nervous and Mental Disease, New York

90: 297-428 (Sept.) 1939

Form of Congenital Myotonia in Goats. S. L. Clark, F. H. Luton and Jessie T. Cutler, Nashville, Tenn.—p. 297.
Reactions and Behavior of Schizophrenic Patients Treated with Metrazol and Camphor. B. Glueck and N. W. Ackerman, Ossining, N. Y.—p. 310.
Induction of Seizures by Closing of Eyes, or by Ocular Pressure, in a Patient with Epilepsy: Case Report. L. J. Robinson, Palmer, Mass.—p. 333.
*Preliminary Observations on Course of Traumatic Psychoses. P. Hoch, New York, and E. Davidoff, Syracuse, N. Y.—p. 337.
Unilateral Torsion-Dystonia: Clinicohistologic Study: Case. R. Gordin, Helsingfors, Finland.—p. 344.
Death Associated with Metrazol Therapy: Report of Case. R. M. Fellows and F. Koenig, Osawatomie, Kan.—p. 358.

Course of Traumatic Psychoses.—In order to ascertain the prognosis and ultimate fate with regard to patients who became psychotic following head injury, Hoch and Davidoff investigated the records of 251 consecutive cases of traumatic psychoses. The preponderance of cases in males (205) is due to the more frequent exposure of men to trauma and in part to occupational causes. Many of the traumatic psychoses were not psychoses due purely to the trauma alone but were associated with other conditions. Of the total number of cases 117 were complicated, in order of their frequency, by alcohol, cerebral arteriosclerosis, senility, neurosyphilis and other miscellaneous conditions such as mental deficiency and epilepsy. These complicating factors are of prognostic importance, as the prognosis is graver in these cases than in those in which no complicating factor exists. Senility and cerebral arteriosclerosis offer the gravest prognosis. The outlook is possibly rendered less hopeful in those cases in which there is an antecedent disturbance to the cerebral circulation. Besides the foregoing complicating concomitants there is another factor which has not been stressed sufficiently in relation to the traumatic psychosis group. An important prognostic determinant is the previous personality organization of the patient who has sustained an injury to the head. Of the schizoid personalities, 75 per cent were definitely unimproved. For patients more of the syntoid type, the prognosis was far better and the percentage of recovery and improvement greater. The ratio of unimprovement in the introvert type as compared to the extrovert type was approximately 2:1. Hallucinations and delusions were present in many cases but were not accompanied by neurologic phenomena characteristic of cortical or subcortical lesions. In the absence of these signs, it would be very difficult to attempt any localization of these psychic manifestations. While it is commonly known that hallucinations and delusions may occur in transitory form in any organic psychosis during the delirious state, they tend to disappear in concomitance with the improvement or recovery of a patient from the confusion or clouded state. In the traumatic psychoses, however, an important feature has been that a patient with a schizoid or introvert makeup regains his mnestic functions and the approximate lucidity of his prepsychotic intellectual state but unharmoniously retains the hallucinations and delusions. Other factors no doubt enter into the clinical picture of the more protracted cases. In addition to the stresses and strains to which the patient is exposed and his reaction to change and thwartings, to financial and family situations, to occupation and to the important questions of compensation and litigation, attention should be focused on the previous personality makeup and what bearing this has on how the individual reacts to the situation. Also it is likely that study of the personality would greatly aid in the understanding of traumatic neuroses.

Journal of Pharmacology & Exper. Therap., Baltimore

67: 1-126 (Sept.) 1939. Partial Index

Action of Sympathomimetic Amines in Cyclopropane, Ether and Chloroform Anesthesia. O. S. Orth, M. D. Leigh, C. H. Mellish and J. W. Stutzman, Madison, Wis.—p. 1.
Pharmacology of Trimethyl Bismuth. T. Sollmann and J. Seifter, Cleveland.—p. 17.
Analeptic Potency of Sympathomimetic Amines. M. L. Tainter, L. J. Whitsell and J. M. Dille, San Francisco.—p. 56.
Action of Sulfapyridine (2-Sulfanilyl Aminopyridine). H. M. Powell and K. K. Chen, Indianapolis.—p. 79.
Toxicity, Fats and Excretion of Propylene Glycol and Some Other Glycols. P. J. Hanzlik, H. W. Newman, W. Van Winkle Jr., A. J. Lehman and N. K. Kennedy, San Francisco.—p. 101.
General Metabolic and Glycogenic Actions of Propylene Glycol and Some Other Glycols. P. J. Hanzlik, A. J. Lehman, W. Van Winkle Jr., and N. K. Kennedy, San Francisco.—p. 114.

Kentucky Medical Journal, Bowling Green

37: 377-422 (Sept.) 1939

Responsibility of the Physician in Lunacy Inquests. J. G. Wilson, Frankfort.—p. 377.
Clinical Diagnosis in General Practice. T. A. Griffith, Mount Vernon.—p. 381.
Exhibits of the A. M. A. at St. Louis, May 1939. M. Casper, Louisville.—p. 385.
Endocrine Therapy in Gynecology and Obstetrics. S. S. Gordon, Louisville.—p. 392.
Annular Skin Lesions of Body Mistaken for Ringworm Infections. W. U. Rutledge, Louisville.—p. 396.
Treatment of Infected Wounds. J. E. Hamilton, Louisville.—p. 398.
Treatment of Carbuncles. A. D. Willmoth, Louisville.—p. 402.
Some of Newer Drugs and Their Uses. D. T. Roberts, West Point.—p. 406.
Armamentarium of Cardiac Therapy. M. M. Weiss, Louisville.—p. 409.
Hydronephrosis. L. Atherton, Louisville.—p. 412.

Maine Medical Association Journal, Portland

30: 213-246 (Sept.) 1939

Hip Nailing. G. M. Morrison, Boston.—p. 213.
Traumatic Shock. F. G. Balch Jr., Boston.—p. 216.
Anesthesia for Traumatic Surgery. S. C. Wiggin, Boston.—p. 219.
Tracheotomy: Bronchoscope as Aid in Emergency Cases. E. L. Pratt, Lewiston.—p. 222.

Michigan State Medical Society Journal, Lansing

38: 741-836 (Sept.) 1939

Opportunities for Continuous Medical Education in Wayne County. R. B. Allen, Detroit.—p. 759.
Congenital Dislocation of Hip. F. C. Kidner, Detroit.—p. 762.
Pyometritis Associated with Metromenorrhagia. C. B. Loranger, Detroit. —p. 768.
Limitations of Transurethral Prostatectomy. R. M. Nesbit, Ann Arbor. —p. 770.
Nontuberculous Pneumothorax Proved by Autopsy: Case. R. L. Fisher, Detroit.—p. 774.

Military Surgeon, Washington, D. C.

85: 197-276 (Sept.) 1939

Syphilis and Mobilization. W. F. Lorenz and W. J. Bleckwenn.—p. 197.
Activities of Military Surgeons in International Congresses of Military Medicine and Pharmacy. W. S. Bainbridge.—p. 211.
Oral Pain as Factor in Diagnosis. H. B. Dierdorff.—p. 216.
Treatment of Lobar Pneumonia with Serum and Sulfanilamide. H. P. Marvin and E. P. Campbell.—p. 224.
Army Medicodental Relationship. W. I. French.—p. 232.
Anxiety Neurosis. M. E. Segal.—p. 239.
Cold and Heat Therapy in Dentistry. C. C. Ellison.—p. 241.

Minnesota Medicine, St. Paul

22: 595-666 (Sept.) 1939

Tuberculosis Problem Viewed in the Light of Recent Pathologic Studies. H. C. Sweany, Chicago.—p. 595.
Treatment of Vaginal Discharges. E. D. Plass, Iowa City.—p. 610.
Placenta Accreta. J. C. Feuling, Bovey.—p. 615.
Cerebral Calcification (Parkes Weber-Dimitri Type). G. R. Kamman, St. Paul.—p. 618.
Parenteral Administration of Fluids: Principles and Indications in Surgical Treatment. M. A. Falconer, Rochester.—p. 621.
*Carbon Monoxide: A Public Health Hazard. L. B. Franklin, Minneapolis.—p. 628.
The Medical Library: A Laboratory for the Literary Physician. T. E. Keys, Rochester.—p. 633.
Traumatic Inguinal Hernia. S. R. Maxeiner and H. E. Hoffert, Minneapolis.—p. 636.
Pseudodiaphragmatic Shadow Due to Pleural Fluid. O. Lipschultz, Minneapolis.—p. 638.

Public Health Hazard of Carbon Monoxide.—The hazards of carbon monoxide to public health are discussed by Franklin, who states that ordinarily it does not appear in nature but results almost entirely from incomplete oxidation of carboniferous material. It has been reported to have been formed in large amounts during severe electrical storms and to have been produced by growing kelp. It is present when buildings burn, is produced in lime, brick and charcoal kilns, is present following explosions and fires in mines and it is also produced on detonation of high explosives. In the laboratory it is produced by heating formic or oxalic acid with sulfuric acid. It is found in smoke and in compartments which have been painted with oil paints and sealed. It has even been reported formed from burning cigarets. About 16 per cent of coal gas is carbon monoxide, 28 per cent of blast furnace stack gas, from 1 to 8 per cent of mine air after dust explosions is carbon monoxide and about 7 per cent of the exhaust from automobile motors. The author points out that 5 per cent of the cars tested on the highways by Van Deventer showed a dangerous concentration (0.03 per cent or more) of carbon monoxide in the air that the driver breathed. The public should be educated on all phases of the hazard, and especially those likely to come in contact with a high concentration of carbon monoxide, such as firemen and policemen. It should be able to recognize symptoms, know the incidence and be able to give first aid. Statistics should be compiled and made available to the public. Methods of accurately detecting injurious amounts of the gas in air should be developed and the public educated in detecting the gas in homes, garages, motor cars and other places. A possible solution of this point could be that the gas companies when installing gas in a home or apartment be required to supply each patron with a piece of apparatus for detecting leaking gas. There should be more experimentation to determine better methods of treatment. Legislation should be enacted for the elimination of the hazard in factories, public garages, mines and wherever there are employees. Such legislation should be supplemented by regular inspection under public health jurisdiction.

Missouri State Medical Assn. Journal, St. Louis

36: 353-382 (Sept.) 1939

Late Advances in Diseases of Pancreas. W. H. Cole, Chicago.—p. 353.
The Female Sex Hormones: A Digest. F. H. Scharles and A. Sophian, Kansas City.—p. 359.
Ophthalmia Neonatorum. L. C. Drews, St. Louis.—p. 366.
Loss of Eyesight in Children Due to Refractive Errors and Crossed Eyes. W. L. Post, Joplin.—p. 368.
Congenital Syphilis and Its Effect on Eyesight. P. S. Luedde, St. Louis. —p. 371.
*Causes and Prevention of Blindness in Adults: Role of the General Practitioner. J. McLeod, Kansas City.—p. 372.
Industrial Eye Injuries and Hazards: Their Prevention and Treatment. R. E. Mason, St. Louis.—p. 373.
Conservation of Eyesight. C. P. Dyer, St. Louis.—p. 374.

Blindness in Adults.—In discussing the prevention of blindness in adults, McLeod examines a typical set of statistics, the tabulation of 11,852 cases of blindness in Pennsylvania. When all congenital anomalies, for which treatment is of little avail in any case, traumatism, all external infections (except gonorrheal conjunctivitis but excluding ophthalmia neonatorum) and all predominantly juvenile diseases are excluded a total of 8,779 cases remains. If ulcerative keratitis (194) is also eliminated on the assumption that all cases were due to external infection and all cases of senile cataract (2,666) there remain 5,919 cases of blindness due to general disease. It is questionable if senile cataract should be omitted, since under this diagnosis were classified all cases of diabetes in which the cataracts developed after the age of 50 and since complete blindness with cataract depends on some retrolenticular disturbance. Breaking down this figure of 5,919 cases due to general disease gives the following incidence: uveitis (all causes) 25.3 per cent, choroiditis 8.2 per cent, chronic glaucoma 24.8 per cent, acute glaucoma 1.9 per cent, vascular diseases (including diabetic and nephritic retinitis) 10.6 per cent, optic atrophy 20.3 per cent and neuroretinitis 5 per cent. This group makes up a total of 96.1 per cent of the 5,919 cases. If from this group glaucoma is excluded there is still 69.4 per cent of these cases (approximately 35 per cent of the total number) the origin of which lies in some systemic condition with focal infection, vascular disease, syphilis and tuberculosis predominating. The importance of watching for early optic nerve changes in syphilis cannot be too strongly emphasized. Here, as in glaucoma, the disease may progress to a dangerous point before visual acuity is noticeably diminished, particularly if the patient is not too intelligent. Recognition of the possible causal agents of certain eye conditions, notably iritis and uveitis, is of great help in searching for the probable factor (usually focal infection or syphilis) responsible for them. Knowledge of the ophthalmologic pictures in chronic diseases involving the vascular systems is of help in formulating the diagnosis and prognosis of these conditions. Nothing can be done about them by local measures and their treatment resolves itself into treatment of the underlying disease.

New England Journal of Medicine, Boston

221: 367-402 (Sept. 7) 1939

Carcinoma of Fallopian Tube. L. Parsons, Boston.—p. 367.
Evolution of Treatment of Pulmonary Tuberculosis at the Rutland State Sanatorium. P. Dufault, Rutland, Mass.—p. 374.
Calculus Formation in Urethral Diverticulum in a Woman: Report of Case. E. A. Gaston and J. Ferrucci, Framingham, Mass.—p. 379.
*Meningitis Due to Micrococcus Tetragenus: Report of Case with Recovery Following Treatment with Sulfanilamide. M. Criscitiello Jr., Pittsfield, Mass.—p. 383.
Radiation Therapy. R. Dresser, Boston.—p. 386.

Meningitis Due to Micrococcus Tetragenus.—Criscitiello reports a case of meningitis due to Micrococcus tetragenus with recovery. A lumbar puncture was done, and the morphology, the staining reaction and the cultural characteristics of the organisms were consistent with those of Micrococcus tetragenus. Ordinarily this organism is found in the nose and throat, where it is not considered to be pathogenic. Although this patient gave no history of infection of the upper part of the respiratory tract, it is likely that the organism gained entrance to the central nervous system from the right ethmoid sinus. Therefore, one should carefully examine the upper part of the respiratory tract for possible foci of infection in these cases. A blood culture was not done on the day of admission. Although one taken seven days later was negative, the patient had already been taking sulfanilamide for five days. The author is of the opinion that in this type of meningitis one is not deal-

ing with a virulent type of organism and that if the patient can b kept alive until he has manufactured enough immune bodies he will recover. Were the author again faced with the same situation, he states that he should look for possible foci of infection in the upper part of the respiratory tract, give supportive treatment, do a lumbar puncture as often as indicated by the patient's condition and give sulfanilamide in adequate doses.

New Orleans Medical and Surgical Journal

92: 113-170 (Sept.) 1939

The Medical Profession: A Businessman's Point of View. E. D. Rapier, New Orleans.—p. 113.
Toxic Effects of Sulfanilamide and Sulfapyridine. C. Brooks, New Orleans.—p. 115.
Emotional Factors in Disease. T. A. Watters, New Orleans.—p. 118.
Diagnostic Survey of the Allergic Patient. N. K. Edrington, New Orleans.—p. 125.
The Eye and Its Care. L. F. Gray, Shreveport, La.—p. 131.
Use of Anatomicophysiologic Incision in Appendicitis. H. S. Coon, Monroe, La.—p. 135.
Diagnosis and Treatment of Diabetes. M. Gardberg, New Orleans.—p. 137.
Management of Diabetic Acidosis and Diabetic Coma in a General Hospital. H. J. Frachtman, New Orleans.—p. 143.
Bacillus Pyocyaneus Meningitis: Report of Six Cases. R. A. Wise and J. H. Musser, New Orleans.—p. 145.

New York State Journal of Medicine, New York

39: 1707-1816 (Sept. 15) 1939

*Treatment of Types V, VII and VIII Pneumococcus Pneumonia with Rabbit Antipneumococcus Serum. E. H. Loughlin, R. H. Bennett and S. H. Spitz, Brooklyn.—p. 1713.
Treatment of Type III Pneumococcus Pneumonia with Sulfanilamide. R. H. Bennett, S. H. Spitz and E. H. Loughlin, Brooklyn.—p. 1722.
Industrial Low Back from Orthopedic Standpoint. S. Kleinberg, New York.—p. 1725.
Neurologic Aspects of Backache. E. D. Friedman, New York.—p. 1734.
Herniation of Nucleus Pulposus and Hypertrophied Ligamenta Flava. D. M. Bosworth and C. C. Hare, New York.—p. 1739.
Unidentified Micro-Organism Resembling Bacillus Lignieri and Pasteurella Pseudotuberculosis, Pathogenic for Man. J. I. Schleifstein and Marion B. Coleman, Albany.—p. 1749.
Evaluation of Laughlen Test in Diagnosis of Syphilis: Report Based on 2,005 Tests. J. Churg and N. Sobel, New York.—p. 1754.
Indications for Estrogen Therapy: Including a Preliminary Report on Use of Two New Estrogen Preparations (Estradiol Dipropionate and Diethyl Stilboesterol) and Subcutaneous Implantation of Crystalline Estradiol Benzoate. S. H. Geist and U. J. Salmon, New York.—p. 1759.
Dispensary Diabetics. A. H. Terry Jr. and S. Folk, New York.—p. 1768.
Some School Hearing Surveys, Analysis and Observations. E. M. Freund, Albany.—p. 1770.
Treatment of Acute Encephalitis by Intravenous Injection of Hypotonic Salt Solution. G. M. Retan, Syracuse.—p. 1774.
Vaccine Therapy in the Rheumatic Patient. H. Weiner, Brooklyn.—p. 1786.
Evaluation of Sulfanilamide Therapy in Acute Otitis Media and Mastoiditis. J. C. Scal, New York.—p. 1790.
Irradiation as Adjunct to Surgery in Substernal Thyroid: Response of Recurrent Fetal Adenoma. I. I. Kaplan and S. Rubenfeld, New York.—p. 1795.

Rabbit Serum for Pneumonia.—Loughlin and his colleagues used unconcentrated and refined rabbit antipneumococcus serum in the treatment of forty-one patients with pneumonia due to the type V pneumococcus, forty-six due to the type VII organism and thirty-eight with type VIII pneumonia. In the first group the pneumonia had been present for an average of ninety hours, with extremes of twenty-six and 192 hours, before rabbit serum was administered. Nine patients had bacteremia when first seen. The average dose of rabbit serum was 290,000 units, and crisis occurred in an average of fourteen hours. Forty patients recovered, and one died. This patient, who was not given serum until 120 hours after onset, died apparently during a thyroid crisis. Thirty-two patients, six of whom had bacteremia, were successfully treated with one dose. In these patients, crisis occurred in an average of eight and one half hours; the average single dose was 246,000 units. The blood stream was sterilized in every instance after the administration of the projected dose. Serum sickness developed in eleven patients. In the patients with pneumonia due to pneumococcus type VII the disease had been present for an average of eighty-three hours, with extremes of twenty and 192 hours, before rabbit serum was administered. Sixteen patients had bacteremia on admission. The average amount of rabbit serum given was 340,000 units. Crisis occurred in an average of fifteen hours. Forty-four patients recovered and two died. In these two fatal cases a severe bacteremia was found and serum therapy was delayed until ninety-six and 144 hours, respectively. One patient was moribund on admission, had pulmonary edema and died within twelve hours after treatment with serum was begun. Thirty-six patients, seven of whom had bacteremia, were successfully treated with one dose. In these patients, crisis occurred in an average of nine and one half hours; the average single successful dose was 279,000 units. The blood stream was sterilized in every instance after the projected dose. Serum sickness developed in nine patients. In the remaining thirty-eight patients the type VIII pneumonia had been present for an average of seventy-nine and one half hours, with extremes of fifteen and 336 hours, before rabbit serum was administered. Twelve patients had bacteremia on admission. The average amount of rabbit serum given was 300,000 units. Crisis occurred in an average of twelve hours. All the patients recovered. Thirty-four patients, of whom nine had bacteremia, were successfully treated with one dose. In these patients, crisis occurred in an average of ten hours; the average single successful dose was 269,000 units. The blood stream was sterilized in every instance after the administration of the projected dose. Serum sickness developed in nine patients. This generally consisted of fever, urticaria and arthritis. These symptoms usually were mild or moderate in severity, although in a few instances a rather severe arthritis was noted. There were no instances of lymphadenitis. The authors conclude that the effectiveness of any therapy in pneumonia depends on (1) the rapidity with which it can destroy the pneumococci in the tissues of the lung and in the blood stream, (2) how quickly it can neutralize the toxins and reduce the toxemia, (3) the rapidity with which it can supply pneumococcus antibodies or stimulate their formation and (4) the absence of untoward reactions that would endanger the patient's life. They find that the homologous unconcentrated and refined rabbit antipneumococcus serum fulfils these requirements in the treatment of types V, VII and VIII pneumonia.

Ohio State Medical Journal, Columbus

35: 913-1032 (Sept.) 1939

Present Status of Silicosis. A. J. Lanza, New York.—p. 929.
Fainting Attacks: Mechanism and Treatment of Certain Clinical Types. E. B. Ferris Jr., Cincinnati.—p. 933.
End Results Following Common Duct Obstruction. F. M. Douglass, Toledo.—p. 938.
Vitamins in Ophthalmology and Otolaryngology: Review of Recent Experimental and Clinical Observations. W. H. Evans, Youngstown.—p. 944.
Facts and Theories of Nasal Disease. R. J. Frackelton, Lakewood.—p. 949.
Statistical Study of Alcoholic Psychoses. N. W. Kaiser, Toledo.—p. 952.
Exploded Theories of Ovulation: Various Notions on When Ovulation Occurs and Their Bases. R. D. Bryant, Cincinnati.—p. 955.
Important Features in Treatment of Fractures. A. F. Voshell, Baltimore.—p. 959.
Acute Abdominal Pain. E. A. Marshall, Cleveland.—p. 966.
Allergy and Nutrition. J. Forman, Columbus.—p. 973.

Pennsylvania Medical Journal, Harrisburg

42: 1425-1648 (Sept.) 1939

Syphilis Acquired from Transfusion and Its Control. F. J. Eichenlaub and R. Stolar, Washington, D. C.—p. 1437.
Rational Application of Sulfanilamide Therapy to Streptococcic Infections. J. S. Lockwood, Philadelphia.—p. 1444.
Mechanism and Management of Surgical Shock. N. E. Freeman, Philadelphia.—p. 1449.
Scope and Problems of Plastic Surgery. H. May, Philadelphia.—p. 1453.
Growth in Diabetic Children. J. H. Barach, Pittsburgh.—p. 1459.
Chemotherapy in Treatment of Urinary Tract Infections. S. H. Johnson 3d, Pittsburgh.—p. 1468.
Chemotherapy in Septicemia. F. G. Harrison, Philadelphia.—p. 1473.
Chemotherapy of Gonorrhea in the Male. F. P. Massaniso and F. S. Schofield, Philadelphia.—p. 1476.
Treatment of Tuberculosis in the Commonwealth of Pennsylvania. Edith MacBride-Dexter, Sharon, and M. Behrend, Philadelphia.—p. 1481.
Role of the Pediatrician in Relation to Surgery. J. Crump, Philadelphia.—p. 1492.
Etiology of Hydronephrosis. B. C. Blaine, Pottsville.—p. 1498.

Public Health Reports, Washington, D. C.

54: 1587-1624 (Sept. 1) 1939

"Influences" of Breast Cancer Development in Mice. J. J. Bittner.—p. 1590.
Influence of Foster Nursing on Incidence of Spontaneous Breast Cancer in Strain C³H Mice. H. B. Andervont and W. J. McEleney.—p. 1597.
Effects of Ox Bile and Estrin on Development of Tumors in Mice. F. C. Turner.—p. 1603.

54: 1625-1662 (Sept. 8) 1939

Dental Programs Sponsored by Health Agencies in Ninety-Four Selected Counties. J. W. Mountin and Evelyn Flook.—p. 1625.
Solubility of Lead Arsenate in Body Fluids. L. T. Fairhall.—p. 1636.
Breast Cancer and Pedigree Relationship of Fostered A Stock Mice. J. J. Bittner.—p. 1642.

Rhode Island Medical Journal, Providence

22: 147-160 (Sept.) 1939

Selection of Patients for Surgery. E. C. Cutler, Boston.—p. 147.

South Carolina Medical Assn. Journal, Greenville

35: 217-242 (Sept.) 1939

Acute Intussusception with Intermittent Spontaneous Reduction and Recurrence. R. F. Zeigler Jr., Seneca.—p. 217.

Review of Cesarean Sections in Greenville County. R. M. Dacus Jr., Greenville.—p. 219.

Southern Medical Journal, Birmingham, Ala.

32: 891-982 (Sept.) 1939. Partial Index

Compound Fractures and Their Treatment. A. T. Moore and J. T. Green, Columbia.—p. 891.

Orthopedic Care of Convalescent Poliomyelitis: Report of Sixty-Three Cases One Year Following Acute Onset. W. V. Newman, Little Rock, Ark.—p. 900.

Metastatic Cancer in Lymph Nodes of Neck. H. G. F. Edwards, Shreveport, La.—p. 905.

Cancer of Larynx and Its Treatment by Total Laryngectomy. S. Israel, Houston, Texas.—p. 911.

Sickle Cell Anemia with Cerebral Thrombosis. A. I. Josey, Columbia, S. C.—p. 915.

Extragenital Granuloma Venereum: Report of Case. E. R. Pund, A. D. Smith, D. Y. Hicks and R. B. Dienst, Augusta, Ga.—p. 917.

Congenital Factor in Acquired Diverticulosis of Jejunum and Ileum. G. H. Bunch, Columbia, S. C.—p. 919.

Head Injuries. A. W. Adson, Rochester, Minn.—p. 926.

Treatment of Congenital Syphilis with Intravenous Arsenical: Analysis of 204 Clinical Cases. J. K. Howles, New Orleans.—p. 940.

Purpura Annularis Telangiectodes: Report of Two Additional Cases. E. R. Hall and V. A. Hall, Memphis, Tenn.—p. 953.

*Nonpollen Factors Simulating Seasonal Respiratory Allergy. H. E. Prince, Houston, Texas.—p. 956.

Industrial Hygiene as a Function of a State Department of Health. G. W. Cox and C. A. Nau, Austin, Texas.—p. 960.

Nonpollen Factors Simulating Seasonal Allergy.—Prince discusses some of the so-called miscellaneous factors that have been so important in several of his cases that they must be regarded as the primary excitants in what otherwise appeared to be true pollinosis; in other instances they have assumed equal importance with pollens in determining seasonal symptoms. As a basis for this report he has selected 150 patients with respiratory allergy studied during the past two years. Of these, ninety-two have symptoms in one or more well defined seasons and fifty-eight have definite yearly seasonal exacerbations. Symptoms of this group are distributed as follows: asthma thirty-eight, hay fever seventy-five and hay fever and asthma thirty-seven. Grass is the most important seasonal inhalant factor (91 per cent) encountered in the spring, followed by trees with 58 per cent. But also 54 per cent of the spring patients reacted to air-borne molds, 71 per cent to danders, 83 per cent to house dust and 25 per cent to orris root, while only 5 per cent reacted to pyrethrum. Similarly 92 per cent of summer patients reacted to grass, and almost as many to house dust (88 per cent) and danders (66 per cent) as in the spring group. However, the percentage of mold reactions is 75, compared with 54 for the spring; orris root is about the same (28 per cent) and pyrethrum is increased to 17 per cent. In the fall group 90 per cent reacted to ragweed, 72 per cent to grass and 26 per cent to chenopodiales; to other factors, reactions occurred as follows: dust 90 per cent, molds 68 per cent, danders 62 per cent, orris root 21 per cent and pyrethrum 7 per cent. In the winter only 35 per cent reacted to pollens (trees), while 98 per cent were sensitive to house dust; 77 per cent reacted to danders, 66 per cent to molds, 35 per cent to orris root and 14 per cent to pyrethrum. In none of the four major seasons, then, can pollens be considered as the entire cause of symptoms. Therefore more attention should be given nonpollen factors which may complicate what appear to be simple cases of seasonal allergy.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

47: 507-560 (Sept.) 1939

Relationship Between Cause and Distribution of Spasticity in Childhood. S. F. Stewart, Los Angeles.—p. 507.

Infective Prostatitis: Critical Review. W. R. Jones, Seattle.—p. 511.

Mucocele of Appendix: Report of Twelve Cases. J. C. Doyle, Beverly Hills, Calif.—p. 515.

Treatment of Severe Thyrotoxicosis. W. O. Thompson, S. G. Taylor 3d, R. W. McNealy and K. A. Meyer, Chicago.—p. 522.

Recurrent Toxic Goiter. R. F. Bowers, New York.—p. 536.

Surgical Approach to Hypertension: Division VIII. F. M. Findlay, San Diego, Calif.—p. 543.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Experimental Pathology, London

20: 297-370 (Aug.) 1939

Purification of Diphtheria Toxoid. C. G. Pope and F. V. Linggood.—p. 297.

Effect of Foreign Tissue Extracts on Efficacy of Influenza Virus Vaccines. C. H. Andrewes and W. Smith.—p. 305.

Experimental Acute Perchloride Intoxication. G. L. Montgomery.—p. 316.

Purification of Insect-Transmitted Plant Viruses. F. C. Bawden and N. W. Pirie.—p. 322.

Pantothenic Acid and Growth of Streptococcus Haemolyticus. H. McIlwain.—p. 330.

Glutamine and Growth of Bacteria. P. Fildes and G. P. Gladstone.—p. 334.

Extravascular Development of Monocyte Observed in Vivo. R. H. Ebert and H. W. Florey.—p. 342.

Metabolism of Lactic Acid in Diphtheritic Toxemia. C. R. Dawson and E. Holmes.—p. 357.

British Journal of Urology, London

11: 207-304 (Sept.) 1939

Cysts of Kidney Due to Hydrocalycosis. K. H. Watkins.—p. 207.

*Role of Vitamin A Deficiency in Etiology of Renal Calculus. H. Long and L. N. Pyrah.—p. 216.

Pyelographic Reactions. T. Moore.—p. 233.

Vitamin A Deficiency and Renal Calculus.—Long and Pyrah studied twenty-five cases of upper urinary lithiasis for vitamin A deficiency together with sixty-five control subjects drawn from healthy people of different economic grades of society. Whereas 75 per cent of the control subjects gave a normal dark adaptation reading, only 36 per cent of the patients who had suffered from urinary lithiasis showed normality. The reading of the remaining 25 per cent of the normal individuals fell just short of the required standard of normality. There were no definitely subnormal readings, whereas among the 64 per cent of the patients suffering from urinary lithiasis 24 per cent were slightly subnormal and 40 per cent were definitely subnormal. After concentrated vitamin A therapy (13,000 units daily for four or five weeks) given to selected patients, 42 per cent gave normal and 58 per cent subnormal readings. One or two patients showed a slight improvement, but this proportion was small and 33 per cent remained definitely subnormal. Therefore dietary deficiencies alone cannot account for the differences in readings between the selected patients and the control subjects, and it would certainly appear from the results that a low body reserve of vitamin A is commoner among patients who had had a urinary calculus even at some interval after operation than among other ordinary healthy members of the community. The results are somewhat similar to those of Ezickson and Feldman, and of Higgins, although the authors state they are not so definite. Too much importance must not be attributed to the vitamin A deficiency found among the 40 per cent of the patients with urinary lithiasis. The general evidence and the results point to this deficiency as only a contributory part in the etiology of urinary lithiasis. At the same time it is interesting that a course of vitamin A therapy had such poor results in raising the vitamin A reserves among the patients, when it is known that such therapy among people who are suffering from dietary deficiencies can usually effect improvement in two or three weeks. Various explanations have been advanced to explain these facts. The deficiency might be explained by excretion of vitamin A in the urine. The deficiency and its apparent inability to be remedied by the oral administration of the vitamin may be perhaps the result and not the cause of the disease and may be related to impairment of kidney function which may be found in some of these patients. This hypothesis the authors believe is worth further investigation. Those selected patients with a short clinical history and no evidence of derangement of kidney function and those with either slight or no infection of the urine before operation usually gave normal readings. On the other hand, those with a long clinical history with its possible effects on the kidney tissue or those who presented evidence of long standing chronic urinary infections, with blood, albumin and bacteria in the urine before operation, generally gave definitely subnormal readings. If this hypothesis were true, it would also provide an explanation for the normal dark adaptation reading of some of the patients

and for the lack of improvement among the subnormal ones after vitamin A therapy. The urine of eight definitely subnormal patients was tested for the presence or absence of vitamin A and also any obvious evidence of impaired kidney function was observed. This investigation failed to show any definite evidence of gross renal damage and in no case was vitamin A to be found in the urine. It seems, therefore, that loss of vitamin A by excretion in the urine cannot account for the low vitamin A reserves found in these cases of renal calculi, and it would appear that the deficiency is more likely to be correlated, as already postulated by Jeghers and Moore, with some defect in the metabolism of the patient or with an inability to absorb the vitamin from the diet. Nevertheless, it is the authors' intention to continue with these investigations on similar patients before operation so that the degree of the importance of this vitamin A deficiency in urinary lithiasis can be interpreted more exactly.

Edinburgh Medical Journal

46: 581-612 (Sept.) 1939

Disseminated Sclerosis: Review of Modern Work on Its Etiology. A. J. Rhodes.—p. 581.
Periodicity of Influenza. J. H. D. Webster.—p. 591.

Indian Medical Gazette, Calcutta

74: 449-512 (Aug.) 1939

Rat Bite Fever in Calcutta. R. N. Chopra, B. C. Basu and S. Sen.—p. 449.
Treatment of Lobar Pneumonia with Sulfapyridine. A. Caplan.—p. 451.
*Treatment of Nervous Diseases by Vitamin B1, with Special Reference to Trigeminal Neuralgia: Report of Seven Cases. I. Bakhsh.—p. 456.
Infection with Giardia Lamblia: Its Pathogenicity and Treatment. R. N. Chopra, B. M. Das Gupta, B. Sen and Z. Ahmed.—p. 458.
Difficulties and Dangers in Providing Donors of Blood. S. D. S. Greval and S. N. Chandra.—p. 461.
Chordoma. M. N. De and B. P. Tribedi.—p. 465.
Certain Cyclic Changes Observed in Blood Pictures of Cases of Untreated Anemia Complicating Pregnancy in Tea Estate Coolies. K. P. Hare.—p. 467.
Experimental Malaria Infections in Two Races of Anopheles Stephensi. P. F. Russell and B. N. Mohan.—p. 469.
*Ionizable Iron in Cow's and Mother's Milk. J. C. Pal.—p. 470.
Five Years of Antimalaria Work at Barwadih Railway Settlement. N. Ahmed.—p. 472.
Moniliasis with Secondary Allergic Patch or Monilide: Case. L. M. Ghosh.—p. 476.

Thiamin Chloride for Trigeminal Neuralgia.—Seven cases of trigeminal neuralgia have been treated with thiamin chloride and Bakhsh states that in six of these improvement ranged from 100 (in four) to 30 per cent. The patient who did not respond to this therapy gave a history of syphilis and although the Wassermann reaction was negative he was given a course of mercury and iodides by mouth without any relief. The four patients who were completely relieved received 160, 210, 84 and 90 mg. of thiamin chloride each and in all of them improvement commenced promptly and in two it was complete when only 50 mg. of the vitamin had been given, although treatment was continued for a few days more. The author has also used thiamin chloride in doses of 10 mg. daily in a case of early disseminated sclerosis for more than one month without the slightest improvement. In another case of diabetic polyneuritis, oral and parenteral administration of from 10 to 20 mg. of the vitamin without insulin for one month produced no effect on the sensory changes; in fact, the patient complained of an exaggeration of tingling and burning sensations in the hands and feet. When his urine became sugar free after insulin therapy he was relieved within a few days. Two cases of arsenical neuritis were uninfluenced by prolonged thiamin chloride therapy, although similar dosage in four cases of polyneuritis of unknown origin produced satisfactory results and the improvement was noticeable in the first week of treatment. One patient with nerve deafness did not respond to six weeks of treatment given by mouth as well by injection. The clinical data are too scanty to evaluate its efficacy in all the diseases for which it is advocated but it seems to be of particular value in many forms of polyneuritis. Whether the action of the vitamin is due to its replacing any deficiency or to some other action is not quite clear yet.

Ionizable Iron in Milk.—Pal determined the available iron in ten different samples of cow's milk from a dairy, a local milkman and a local market and two mixed samples of mother's milk. Almost all the iron present in milk is in available form. The average available or ionizable iron content in the cow's milk was 0.635 mg. per hundred cubic centimeters of milk. This is almost equal to the total iron present in the samples. The mean figure for ionizable iron in mother's milk was also almost the same as the total iron present and was found to be 0.625 mg. per hundred cubic centimeters of mother's milk.

Lancet, London

2: 629-674 (Sept. 16) 1939

*Postoperative Thrombosis and Embolism: Mortality and Morbidity. R. Pilcher.—p. 629.
Erythrocytes-Plasma Interface and Consequences of Its Diminution. R. Fåhraeus.—p. 630.
"Influenzal" Meningitis Treated with Sulfapyridine: Report of Two Cases. E. H. Roche and J. E. Caughey.—p. 635.
Valvular Pneumothorax: Treated by Mechanical Valve and Obliterative Pleurisy. F. G. Chandler.—p. 638.
*Iron Administration and Hemoglobin Levels During Pregnancy. E. M. Widdowson.—p. 640.
Prophylactic Inoculation During Incubation Period. H. Schütze.—p. 643.

Postoperative Thrombosis and Embolism.—Pilcher says that a careful study has been made at the University College Hospital in London for cases of thrombosis and embolism. The records of the decade from 1929 to 1938 have been analyzed to show the interrelation of thrombosis and embolism, and the mortality of the latter. Prophylaxis was tried in the series presented, but no specific treatment except embolectomy in one case. Regarding the criteria of diagnosis the author says that in both thrombosis and embolism there is a rise of temperature. In simple thrombosis the rise is seldom of more than 1.5 degrees F., but when embolism occurs the temperature rises higher. The rise of temperature in a case of embolism often precedes the symptoms and may be presumed to be due to undetected thrombosis. The signs on which thrombosis is diagnosed are delayed cooling on exposure, pain and tenderness, edema, slight cyanosis and fulness of superficial veins. Of these the most constant are tenderness and delayed cooling; these in conjunction with a rise of temperature would be regarded as evidence of thrombosis. The signs of thrombosis enumerated were not all present in every case. In the diagnosis of embolism little importance is attached to the presence of recognized thrombosis, and, in fact, in the majority of cases no thrombosis was found. Unless, therefore, gross errors are made in the diagnosis of embolism, it must be accepted that many cases of thrombosis are not diagnosed. The fact that thrombosis may be latent makes it difficult to assess its risks on the evidence of diagnosed cases. Pulmonary embolism in addition to fever has three important features: pain, hemoptysis and signs of pleurisy or consolidation. The 261 cases of thrombosis and embolism that are discussed here are analyzed in several tables. The first table lists ninety-eight cases of femoral or crural thrombosis only, forty-three cases of thrombosis with nonfatal embolism, sixty-eight cases of nonfatal embolism with recognized thrombosis, forty-four cases of fatal embolism and eight cases of thrombosis or embolism which were diagnosed in life but in which death resulted from other causes. The second table analyzes the material from the point of view of association of thrombosis and embolism and the third table lists the mortality rates. The mortality rate of the whole series was 16.8 per cent. The mortality rate of the first attack of embolism was 21.6 per cent. The total mortality rate of embolism was 28 per cent. Fatal embolism followed 4.6 per cent of diagnosed thromboses and 8.1 per cent of diagnosed nonfatal embolisms. This difference is not statistically significant. In the majority of nonfatal embolisms no evidence of thrombosis was found. The majority of fatal embolisms were unexpected. Thrombosis diagnosed in life is commoner on the left side than the right. This is the reverse of the observations in a large postmortem series of fatal embolisms.

Iron and Hemoglobin During Pregnancy.—Widdowson studied the hemoglobin levels of pregnant women before, during and after periods of therapeutic medication with iron. Hemoglobin determinations were made by the Haldane method of 100 women, all of whom were twenty weeks' pregnant or less, attending the antepartum department of King's College Hospital, London. The determinations were repeated a month later. Then half the women (those attending on Wednesdays) were prescribed 1,000 mg. of iron, as ferric ammonium citrate or ferrum reductum, daily for six weeks. The level of hemoglobin

in the capillary blood was determined at fortnightly intervals. The administration of iron was then stopped and the hemoglobin estimated fortnightly until a week after delivery. The other women (attending on Tuesdays) were given no medicine, and their hemoglobin levels were observed at monthly intervals until delivery and again a week later. In both groups an estimation was always made within twenty-four hours after delivery. At the end of the experiment it was decided not to consider (1) women whose babies were born before the thirty-sixth week, (2) women who had taken the last dose of iron within eight weeks of delivery and (3) women in the experimental group who had not taken the prescribed iron. After these omissions thirty-one women were left in the "iron" group and forty-four in the control group. In the control series the characteristic response was a tendency to fall steadily throughout pregnancy and to rise sharply after delivery. The cause of the fall, although possibly in some cases the result of a true deficiency of iron, is probably due largely to a rise in the volume of plasma unaccompanied by a corresponding rise in the number of circulating red blood cells. The responses of the experimental group are much more complicated than those of the control because, besides the effects of pregnancy and delivery common to the two groups, two further stimuli were in operation: (1) the administration of iron and (2) the cessation of its administration. The response to iron was not an instantaneous increase in all the women's hemoglobin concentrations. A few of the hemoglobin curves continued to fall, as though iron had not been given at all; several showed a break in the fall but no real rise, and some of them rose. The cessation of administration of iron led almost always to a fall in the hemoglobin level of those women in whom its administration had initiated a rise. In the discussion the author points out that, whereas the administration of iron has been shown by others to check the fall of hemoglobin during pregnancy, the fall after the administration has been stopped is a new observation and one which is difficult to explain. The tentative explanation offered by him is that one of the many factors regulating the level of hemoglobin in the circulation is the amount of iron in the plasma; the more there is, the more active the marrow cells become. When iron is not being administered, the amount of iron in the plasma is maintained at a low constant level by the high capacity of the storage organs. The administration of iron, however, temporarily raises the plasma iron, which stimulates the marrow to greater activity. It will be noted that this theory emphasizes the amount of iron in the plasma rather than the amount in the body as the regulator of marrow activity. The problem arises: Does the raising of a person's hemoglobin with massive doses of iron prove that the person was in need of iron; i. e., in a pathologic state? It might reasonably be held that, if the hemoglobin fell to its original level when the iron was discontinued, no pathologic state had been disclosed. Against this view must be set the weight of clinical opinion, which has pronounced definitely in favor of raising the hemoglobins of babies and pregnant women.

Medical Journal of Australia, Sydney

2: 303-344 (Aug. 26) 1939

Pott's Disease in Children. G. K. Smith.—p. 303.
Tumors and Malformations of Blood Vessels of Brain and Spinal Cord. L. B. Cox and H. C. Trumble.—p. 308.

Proceedings of Royal Society of Medicine, London

32: 1191-1370 (Aug.) 1939

Town and Country Planning. G. L. Pepler.—p. 1191.
*Familial Hepatitis. F. B. Parsons.—p. 1197.
Diagnostic Value of Hysterography. A. Davis.—p. 1211.
Factors Influencing Attitude of Fetus in Utero. G. F. Gibberd.—p. 1223.
Effects of Stilbestrol on Labor. J. H. Peel.—p. 1230.
Plasma Phosphatase in Jaundice in Children. W. W. Payne.—p. 1265.
Porphyrins and Their Relation to Metabolism of Blood Pigments. C. Rimington.—p. 1268.
Porphyrin Excretion Following Antipyretics. G. Brownlee.—p. 1276.
*Methemalbumin in Man (Pseudomethemoglobin). N. H. Fairley.—p. 1278.

Familial Hepatitis.—Parsons reports familial hepatitis in a family of nine children. Two of the children are alive and well, two are alive and have hepatic enlargement, four have died from hepatic failure and one has died probably of some other cause. No member of the family suffered from icterus neonatorum and in no case has there been any suggestion of retardation of growth. Both parents are alive and well. They have not suffered from relevant illnesses in the past and, so far as can be ascertained, there is no history of hepatic dysfunction on either side. Although necropsies were done on only two members of this family, the appearances observed are common to those of patients dying of cholemia. The picture in one case was that of a perilobular cirrhosis and in the other of a multilobular cirrhosis, but in each case it appeared that an acute hepatic necrosis was superimposed on a chronic hepatitis. No satisfactory evidence was obtained of the ingestion of any substance known to provoke hepatic damage. The incidence of the cases occurring over a period of twenty-two years is against this view. The occurrence of choreiform movements for fourteen months before death in one case and the fact that the disease manifested itself in the second decade of life indicates that the possible diagnosis of hepatolenticular degeneration cannot lightly be dismissed, particularly as the changes in the brain in this condition are not always visible to the naked eye on postmortem examination and that they are sometimes elusive on microscopic examination. The presence of cirrhosis of the perilobular type, the absence of significant changes in the brain and the occurrence of unilateral movements diagnosed as hysterical are, on the whole, not in harmony with a diagnosis of hepatolenticular degeneration, and it would seem that the family should be regarded as an example of familial hepatitis.

Methemalbumin in Man.—Methemalbumin in man, according to Fairley, is formed from extracorpuscular hemoglobin when blood is destroyed in large quantities and remains in the circulation for a sufficient time. During the extracellular catabolism of hemoglobin, the molecule is split into globin and haem. The haem is oxidized to hematin, which promptly unites with serum albumin to form methemalbumin, the latter not passing through the kidney and never appearing in the urine. Recent work by Rimington indicates that hematin injected intravenously produces an increased porphyrin excretion in the feces. It appears that, like bilirubin, methemalbumin is disposed of by way of the liver and would be present in greater concentration in the circulation when intravascular hemolysis was associated with liver disease. This, the author states, he has recently confirmed clinically in cases of cirrhosis of the liver and splenomegaly associated with hemolytic anemia and hemoglobinuria.

Tubercle, London

20: 485-532 (Aug.) 1939

*Sedimentation Rate, White Blood Cell Count and Temperature in Acute Lobar Pneumonia. I. Douglas-Wilson.—p. 485.
Radiologic Examination of Larynx. R. S. Stevenson.—p. 497.
Tuberculous Cervical Lymphadenitis: Epidemiology and Pathogenesis. B. C. Thompson.—p. 504.
Id.: Pathology and Treatment. E. S. Evans.—p. 510.

Sedimentation Rate, Leukocyte Count and Temperature in Pneumonia.—Douglas-Wilson determined the relation between the sedimentation rate, leukocyte count and temperature in forty-four cases of acute lobar pneumonia, in which there were ten deaths. Estimations were made daily throughout the febrile period and at regular intervals thereafter until recovery was complete. The mean sedimentation rate increased from the second (40) to the fourth day (81.38) of illness and then fluctuated around a constant level for the following three days with the maximal figure on the sixth day (82.91), before declining. In the case of the leukocyte count the mean figure fell from the first (187.1) to the sixth day (111.8), whereafter it rose till the ninth day (161.3). A slow decline ensued. Wide fluctuations above and below the average were found both in the sedimentation rate and in the leukocyte count. Body temperature had no influence on the sedimentation rate and leukocyte count. The only statistically significant correlation between the sedimentation rate and the leukocyte count occurred in the first four days of illness, but the trend of the signs of the coefficients suggests that, whereas at first they tend to be inversely related, the tendency in the later days is toward a direct relationship. This was confirmed by calculation of the correlation coefficient for each day by Sheppard's method. The change from inverse to direct variation occurred about the sixth day. In individual cases inverse variation was observed for a period varying with the duration of fever and occasionally persisted up to the tenth day of illness. The maximal, minimal and mean of the sedimentation rate in the fatal cases did not differ greatly from that in the cases in which survival occurred. A fatal outcome

invariably resulted with leukopenia but leukopenia was found in only a half of the fatal cases. In the other half a moderate and even increasing leukocytosis was found. In every fatal case the sedimentation rate began to decrease either two or three days before death, and this decrease continued up to the time of death. This progressive fall of the sedimentation rate, especially when accompanied by a high or rising pulse rate, has been found an excellent guide to the prognosis, resulting on several occasions in the accurate forecast of a fatal outcome which would have been otherwise unforeseen. In bronchopneumonia the same tendency as in lobar pneumonia toward inverse relationship of the sedimentation rate and leukocyte count in the febrile stage has been observed. The sedimentation rate remains increased longer during resolution in bronchopneumonia than in lobar pneumonia. As in lobar pneumonia, the sedimentation rate returned to normal only when resolution was complete.

Chinese Medical Journal, Peiping

56: 1-98 (July) 1939

*Hematuria, Renal Colic and Acetylsulfapyridine Stone Formation Associated with Sulfapyridine Therapy. I. Snapper, S. H. Liu, H. L. Chung, T. F. Yü and H. M. Sun.—p. 1.
Research on Typhus in Shanghai. J. H. Raynal, J. Fournier and E. Velliot.—p. 11.
*Further Studies on Serum Treatment of Typhoid Fever. H. Yü.—p. 29.
Development of Leishmania in Chinese Sandflies Fed on Dogs with Canine Leishmaniasis. L. C. Feng and H. L. Chung.—p. 35.
Natural Infection of Phlebotomus Chinensis in Peiping with Leishmania Flagellates. H. L. Chung and L. C. Feng.—p. 47.
Mosquitoes of Hunan Province, with Special Reference to Anopheles. T. L. Chang.—p. 52.
Plan for Malaria Control in Yunnan. H. Y. Yao.—p. 63.
Tuberculosis in a General Hospital. T. C. Y. Sun and J. C. Thoroughman.—p. 69.

Hematuria, Colic and Calculi After Sulfapyridine Therapy.—Snapper and his associates report the occurrence of hematuria during sulfapyridine treatment both in children and in adults. Of the three adults, the first had asymptomatic hematuria, the second hematuria and colicky pain, and the third hematuria associated with a renal calculus composed of acetylsulfapyridine. Several cases of hematuria in children have been encountered by the authors. They report one in which hematuria developed after thirty-six hours of medication. They believe that the recovery of a sulfapyridine calculus from the urinary tract in man has not as yet been recorded. According to recent experiments on rats, rabbits and monkeys, after continuous therapy with sulfapyridine the urine often shows small concretions consisting of needle-like crystals. These crystals prove to be acetylsulfapyridine. The same process appears to occur in patients treated with the drug. The highly insoluble acetylsulfapyridine which is formed during the metabolism of the drug precipitates in the urinary tracts, giving rise to crops of crystals and eventually to little calculi. Irritation or traumatism by the calculi would result in hematuria with or without renal colic. It is evident that in some cases, as observed by Southworth and Cooke, obstruction of the ureter by these concretions may lead to temporary anuria and nitrogen retention in the blood. Different animal species vary in their susceptibility to urolithiasis as a result of sulfapyridine administration. Whereas monkeys needed 0.25 Gm., rabbits from 10 to 15 Gm. and rats 5 Gm. per kilogram of weight daily for ten days, acetylsulfapyridine calculi developed in one of the patients after he received approximately 0.1 Gm. of sulfapyridine per kilogram daily for nine days.

Serum Treatment of Typhoid.—Yü treated sixty-four cases of typhoid with serum prepared with alcohol killed and live antigens. In thirty-three cases there was an immediate drop in temperature and a decrease in toxic symptoms. In nineteen there was a reduction in toxemia but no noticeable effect on the temperature curve. There was no change in the remaining twelve patients. The study substantiates the previous reports from the Lester Institute and the reports of Felix and other workers that the new antityphoid serum is definitely beneficial. The beneficial effect of this batch of serum on toxemia was more striking and constant than the effect on pyrexia. To date, a total of 305 cases of typhoid have been treated with this new serum. Although the number is still small, the good results obtained in the hands of the various workers justifies its routine employment in typhoid, more especially if toxemic features are in evidence.

Archives des Maladies de l'Appareil Digestif, Paris

29: 697-816 (July) 1939

Complicated Diverticulum of Duodenum. R. Gregoire.—p. 701.
*Primary and Secondary Hypotension and Metabolism of Carbohydrates. H. G. D. Fiszel.—p. 710.
*Lipothymia in Chronic and Latent Appendicitis. A. C. Borcesco and V. Ionescu-Movila.—p. 750.

Hypotension and Carbohydrate Metabolism.—Fiszel says that it was Ferrarini who first directed attention to a morbid entity which he designated as constitutional angiohypotonia and which is characterized by arterial hypotension resulting from deficient tonus in the vascular system and in other tissues. Fiszel says that this form of hypotension is characterized by a more or less pronounced physical and psychic fatigue. Slight exertions exhaust these patients. Moreover, they have frequent painful sensations in the cardiac region such as retrosternal constriction, palpations, sensations of emptiness, feelings of anxiety, and pains radiating toward the left arm. Hypoglycemic crises are known to occur in these cases. The sensations of hunger are suppressed by a small amount of nourishment, especially carbohydrates. Postprandial somnolence is a frequent symptom in these cases and general malaise, vertigo, headaches, dimness of vision, fainting, abnormal sensitiveness to cold on the part of the extremities, acrocyanosis, paresthesias, constipation and painful menstruation are other symptoms often observed. Since the clinical symptoms of hypotonia resemble those of hypoglycemic shock, Fiszel decided to investigate the carbohydrate metabolism of patients with hypotonia by means of sugar tolerance tests. His studies were made on patients with primary hypotonia and on some with secondary hypotonia, forty in all. He designates as secondary that form of hypotonia which is encountered in the course of or after grave diseases such as acute infectious diseases, intoxications and cardiovascular diseases. After describing the characteristics of the blood sugar curves which he obtained in the two forms of hypotonia, he says that the clinical aspects and the studies on the carbohydrate metabolism lead him to conclude that primary hypotonia is the manifestation of an absolute displacement of the neurohormonal factors; that is to say, there exists an augmentation of the tonus of the vagal system and hyperfunctioning of the endocrine glands belonging to the insulin group. Secondary hypotonia is the manifestation of a relative displacement of the hormonal factors, that is, of hypotonicity of the sympathetic nervous system and of hypofunction of the endocrine glands of the adrenal group, or it is the expression of hepatic disturbances or of both hepatic and endocrine perturbations.

Lipothymia in Chronic and Latent Appendicitis.—Borcesco and Ionescu-Movila think that many cases of chronic appendicitis are not recognized because either they do not present symptoms permitting a definite diagnosis or the physician does not think of this disorder. In the course of a long practice, a careful search for symptoms indicative of chronic or latent appendicitis revealed to the authors three which they consider of great value. These are (1) appendicular vertigo, (2) lipothymia (faintness) and (3) urgent diarrheal stools preceded by colics which cease after evacuation. These three symptoms when associated in one case constitute a veritable symptomatic triad valuable for the diagnosis of chronic and especially of latent appendicitis. In this report the authors direct attention especially to the second of the triad of symptoms; namely, to lipothymia or faintness. After giving brief outlines of twenty typical examples of faintness in cases of appendicular lesions, they stress the following points: 1. Lipothymia is a symptom which is of great value for the diagnosis of chronic and latent appendicitis. Studies in 3,000 cases of appendicular lesions revealed it in 244, that is, in 8 per cent. 2. Lipothymia is sometimes associated with vertigo and with urgent diarrheal stools that are preceded by colics which disappear after evacuation. 3. Lipothymia can be considered as a symptom coming on unexpectedly with recurrences of chronic appendicitis, often announcing an appendicular crisis or as the first symptom of the onset of appendicitis. 4. It is important that the physician know the appendicular origin of lipothymia, so that in a case which, apart from other digestive disturbances, presents lipothymia, the possibility of a chronic appendicitis will be taken into consideration.

Journal Belge de Neurol. et de Psychiat., Brussels

39: 607-646 (Sept.) 1939

*Azoman (Triazol) in Therapy of Schizophrenia. H. Hoven.—p. 607.
Korsakoff's Psychosis with Polyneuritis in Course of Postpuerperal Septicemia. M. Maere.—p. 616.
Pneumonococcic Meningitis Cured by Sulfanilamide. E. Evrard and A. Bragard.—p. 622.

Therapy of Schizophrenia.—Discussing the various types of shock therapy of schizophrenia, Hoven says that insulin exerts a favorable effect especially on the paranoid, hallucinatory type of dementia praecox and on catatonic dementia praecox with agitation, whereas metrazol is most effective in stuporous dementia praecox and in late schizophrenia. However, treatment with metrazol presents certain inconveniences. It frightens some patients because it causes anguish and the feeling that death is imminent and so the patients refuse to submit to injection. Attempts have therefore been made to substitute other preparations which do not have the shortcomings of metrazol. In this paper the author discusses the use of azoman, which is known also as triazol and the chemical composition of which greatly resembles that of metrazol. After citing other investigators who have employed this substance, the author says that so far he has used it in twenty-five cases of schizophrenia and that he can confirm the favorable results obtained by others. He says that the substance is available in a 5 per cent aqueous solution and that it can be administered by intravenous or intramuscular injection. In general remarks about the dosage he cites studies by von Braunmühl in which it was determined that for intramuscular injection the dose should be 0.039 cc. of the 5 per cent aqueous solution per kilogram of body weight for men and 0.037 cc. for women; for the intravenous injection the corresponding doses are 0.023 and 0.021 cc. respectively. If a patient is in a hypoglycemic (postinsulin) state the doses are slightly different. The computation of the dose to be injected is not as complicated as it might appear; for instance, to a patient weighing 56 Kg., 1.2 cc. of the solution was administered by intravenous injection and to a patient weighing 59 Kg., 2.2 cc. was given by intramuscular injection. The authors report several cases in which they employed the substitute of metrazol. They reach the conclusion that, if utilized with caution, the new preparation has great advantages and produces good results in schizophrenia.

Presse Médicale, Paris

47: 1285-1300 (Aug. 26) 1939

*Therapeutic Value of Autonomous Pleurotomy. F. Dumarest and P. Pavie.—p. 1285.
Hematoporphyrin Therapy in Pyramidal Hypertonia. W. Sterling and W. Stein.—p. 1287.

Pleurotomy in Artificial Pneumothorax.—Dumarest and Pavie evaluate the advantages of pleurotomy in pleural complications of artificial pneumothorax. In their analysis of the threefold objection to this surgical procedure, namely the dangers of secondary infections, the risks to the organism of prolonged suppuration and the irremediability of thoracic fistulas when once established, they present the following considerations: 1. Pleural infections occur almost entirely in exceptional cases, such as when surgical intervention is performed on cachectic patients as a last desperate measure or when poor drainage causes retention of infective matter. A correctly performed and maintained drainage eliminates, in principle and practice, all infectious evolution. 2. Clinical observations show that pleurotomy is no hindrance to a gradual establishment of excellent well being with a rapid gain in weight and that it does not lead to amylosis. The inconveniences of prolonged suppuration diminish in time. 3. The spontaneous occlusion of fistulas is of frequent occurrence when drainage has not exceeded several months. In thirty-nine recent pleurotomies the authors, jointly with Rougy, their deceased collaborator, could report closing of parietal fistula in eight cases, five with symphysis and three with conservation of the pneumothorax. In their discussion of the advantages of pleurotomy, the authors point out that its pulmonary significance apart from any pleural value lies in the fact that rarely homolateral or contralateral pulmonary evolutions are found in cases in which an effective pleurotomy has been performed. According to the authors, pleurotomy offers the following pulmonary advantages: (1) It protects the opposite lung from infection in the event of perforated pneumothorax and has surprising curative effects on existing contralateral lesions; (2) it completes the collapse of the lung under treatment; (3) it facilitates the occlusion and cicatrization of pleuropulmonary fistulas in intermittent and latent cases in which surgery is performed without delay. Wide, open fistulas, however, persist but are easily endured by the patient if drainage is properly continued. The clinical experiences of the authors, therefore, do not confirm alleged dangers to the pleura and lungs. On the contrary, surgical delay and prolonged pleural lavage may convert an intermittent into a permanent fistula and induce fatal consequences of pulmonary inundation. Nor are tuberculous pleurisies of malignant evolution benefited by puncture and lavage, rapidly becoming cachectic. Open pleural cavities in cases of complete pneumothorax in which infection is maintained by a permanent pleuropulmonary fistula can be stabilized effectively for a long time by pleurotomy. The advantage of pleurotomy over thoracoplasty in pleural infection rests on avoiding the necessity of an early severe operation with its high fatality when the patient is in a precarious condition and in restoring him progressively to the resumption of at least a partial customary activity of life. The inconveniences of permanent drainage receive their proper evaluation in the scale of relative human values in the sentiment expressed by one of the author's patients that it is better to live in ill health than to die while being cured.

Revista Médica Latino-Americana, Buenos Aires

24: 983-1085 (July) 1939. Partial Index

Medical Treatment of Phlegmons of Dental Origin by Neoarsphenamine. J. Beltranena S.—p. 983.
Determination of Bilirubinuria. L. Galindez and E. Vanni.—p. 994.
*Mammography: X-Ray Examination of Milk Ducts by Using Contrast Mediums. A. E. Nogués and C. L. Gazzotti.—p. 999.

X-Ray Examination of Milk Ducts.—Nogués and Gazzotti made an x-ray study of the milk ducts (so-called mammography) of a group of nine women. They resorted to Hicken's technic, which was reported in *Surgery, Gynecology and Obstetrics* in March 1937 and abstracted in THE JOURNAL May 1, 1937, page 1575. The procedure utilizes a contrast substance, which is injected into the milk ducts for x-ray study. The authors used a 30 per cent solution of thorium dioxide sol. They describe in detail and also by illustrations the x-ray aspects of the milk ducts in normal conditions, during lactation and in the presence of mammary or intracanalicular tumors, as well as in the presence of the bloody, white and yellow discharge from the nipple. The authors found that the procedure is harmless if it is carried on by the proper technic. The method has proper indications, namely (1) the diagnosis of intracanalicular tumors or of inflammation of the milk ducts, (2) diagnosis of the intracanalicular tumoral (or nontumoral) origin of the bleeding nipple and (3) the differential diagnosis of various types of white and yellow discharge from the nipple. The authors found that milk ducts which harbor a tumor (papilloma or carcinoma) give mammograms with shadows showing ampullar dilatation and a lacunar image. The nature, either benign or malignant, of the tumor cannot be diagnosed from the aspect of the mammogram. Clinically intracanalicular papilloma shows by the bleeding nipple. Therefore the x-ray appearance of the bleeding nipple from intracanalicular papilloma is that of milk ducts harboring a tumor. Mammograms of breasts with a white or yellow discharge which is due to any of the various types of acute and chronic inflammation of one or several milk ducts, with or without complicating canalicular abscess, are those which correspond to the given type of inflammation and to the evolution of the conditions. The x-ray aspects in the conditions are varied. Generally the mammograms give shadows showing more or less intense ampullar dilatation of the involved ducts or else pseudocavities, retraction and anfractuosities. The mammograms can be differentiated from those of breasts with secretion from the nipple which is due to mammary tumors without involvement of the canalicular system, which shows normal at the mammogram. In the diagnosis of paraductal tumors without involvement of the ductal system, mammography has a secondary value. The seat, form and number of the tumors can be interpreted from the deformation of the ducts from the neighboring tumors. Cancer of the breast can be suspected by

a mammogram which shows deformation of the milk ducts and destruction of the ductal branches as they touch the tumor, which is shown by a dark shadow which absorbs the ductal branches as though the latter were amputated by the former.

Klinische Wochenschrift, Berlin

18: 981-1012 (July 22) 1939. Partial Index

Experimental Investigations on Iodophilia of Leukocytes. F. Hoff and L. Bachmann.—p. 981.
New Objective Criterion for Detection of C-Hypovitaminosis. P. Wördehoff.—p. 984.
Parenteral Dextrose Tolerance Test. F. Axmacher and E. Funke.—p. 984.
*Development of Free Gases in Blood and Tissues in Rapid Decompression. G. Schubert and A. Grüner.—p. 988.
Behavior of Iron Content of Serum During Influenza. P. Büchmann and E. Heyl.—p. 990.
Limits of Metabolic Action in Dentin. T. Spreter von Kreudenstein.—p. 992.

Free Gases in Rapid Decompression.—Schubert and Grüner studied the question of the development of gases in blood and tissues during sudden transition from extremely low to normal atmospheric pressures and aimed to determine whether the danger of gas embolism can be averted by prompt return to normal pressure. A solution of these questions seemed important in connection with flying in the stratosphere. Experiments on rats which were subjected to low atmospheric pressures (70 mm. of mercury) and then were returned to normal pressure gave information about the pathogenesis of atelectasis. The development of gases and gas embolism were likewise investigated on rats as well as on other species of animals (guinea pigs, cats and dogs). The authors show that their experiments give information about the dangers threatening persons who fly at stratospheric altitudes, when the chamber or the pressure suits suddenly become defective. They found that even a brief transition (less than one minute) to pressures between 75 and 70 mm. of mercury, that is, to altitudes of from 16,000 to 17,000 meters, is not necessarily fatal if a return to greater pressures is effected immediately. However, the longer the aviators stay at this pressure, the more extensive are the tears in the pulmonary tissues and the hemorrhages into the alveoli and bronchioles. These represent the life threatening factor, even if the return to normal pressure lasts only seconds, whereas the development of gases represents an entirely reversible process. A stay of more than ninety seconds in pressures of less than 60 mm. of mercury is absolutely fatal, for a return to normal pressure, even for seconds, produces not only a complete atelectasis of the lung but also the development of such quantities of gases that the circulation in the vital organs is at once impaired and remains so permanently. The authors show that there are physiologic and technical protective measures against these dangers. The most effective physiologic one is that as soon as the chamber or the pressure suit become defective a voluntary hyperventilation is begun in order to effect equilibration of pressure between lung and external air and thus avoid tearing of the pulmonary parenchyma and also to reduce the tension differences of gases by increased diffusion. The technical protective measure consists in provision with tanks containing highly compressed oxygen. They should be discharged under high pressure to be regulated automatically by the pressure of the chamber. The same automatic regulation should be provided during steep descent.

Monatsschrift für Kinderheilkunde, Berlin

79: 1-146 (July 6) 1939. Partial Index

Indication for Treatment in Climatic Chamber. S. Liebe.—p. 1.
Suipestifer Infection During Childhood. W. Goeters.—p. 27.
Hepatic Rickets. M. Klotz.—p. 39.
Parenteral Administration of Antirachitic Vitamin. M. Klotz.—p. 43.
Dermographic Manifestations During Childhood. Ruth Hüsgen.—p. 52.
Blood Forming Action of Soy Flour. T. Takuma and K. Sakurai.—p. 62.
*Pathogenesis of Renal Hemorrhages During Diphtheria. H. Stiepel.—p. 67.
Protein Metabolism of Nurslings in Light of Nitrogen and Sulfur Metabolism. P. Ujsághy.—p. 79.

Pathogenesis of Renal Hemorrhages During Diphtheria.—Stiepel points out that hematuria is occasionally observed in cases of diphtheria. Reviewing different opinions about the source of these hemorrhages, he says that Randerath demonstrated in 1933 that renal hemorrhages in diphtheria represent glomerular hemorrhages brought about by capillary impairment and that the appearance of erythrocytes in the urine of diphtheria patients does not permit the conclusion that a glomerular nephritis exists. On the basis of his microscopic studies, Randerath could exclude not only glomerular nephritis but also glomerular irritation and glomerular hemorrhages as the result of stasis, and he interpreted the hemorrhages as the manifestations of impairment of the glomerular capillary walls. He thinks that these hemorrhages can be regarded as equivalent to the cutaneous and to the subserous and subendocardial hemorrhages of diphtheria patients. Since Randerath's conclusions were based on a single observation, Stiepel decided to reexamine his results in a larger number of cases. He made microscopic studies on the kidneys in fifteen fatal cases of diphtheria and, in addition to purely nephrotic changes in the region of the tubules, he observed in eight cases in circumscribed regions of the renal cortex massive hemorrhages into the glomerular capsules and into the lumens of the uriniferous tubules. The author agrees with Randerath that these hemorrhages originate in the glomerular coils and that they are the result of an impairment of the walls of these coils, which in turn is a manifestation of the generalized capillary impairment during diphtheria. The microscopic aspect of all eight cases demonstrate clearly that the presence of erythrocytes in the urine does not permit the conclusion that inflammatory processes exist in the kidney. Their appearance in the urine is only an indication of the severity of the existing capillary changes.

Vrachebnoe Delo, Kharkov

21: 291-370 (No. 5) 1939. Partial Index

Hepatopulmonary System. S. M. Leites.—p. 291.
*Hepatopulmonary Syndrome in Lobar Pneumonia. A. L. Vilkovisky.—p. 293.
Role of Lungs and of Liver in Carbohydrate Metabolism of Lobar Pneumonia. P. M. Perchik.—p. 299.
Alterations of Nitrogenous Component of Serum in Lobar Pneumonia. M. I. Dunaevskiy.—p. 307.
Course of Sedimentation Reaction of Erythrocytes in Lobar Pneumonia Treated by Intravenous Serum. A. G. Korfanti.—p. 313.
Venous Pressure in Pneumonia of Children. L. B. Krasik.—p. 315.

Hepatopulmonary Syndrome in Lobar Pneumonia.—Vilkovisky sensitized rabbits by intravenous injection of horse serum or of a dead culture of pneumococci or streptococci, after which the horse serum was administered either by inhalation or by the intratracheal route, or by the combination of the latter with simultaneous injection of pneumococci into the blood stream. The effect of cooling, analogous to "catching a cold," was likewise estimated. These experiments, carried out on eighty animals, demonstrated the role of the allergic factor in the genesis of lobar pneumonia, the possibility of producing sensitization by various agents, such as heterogeneous proteins, nonspecific or specific micro-organisms, the possibility of producing pneumonia through hematogenous introduction of the infectious agent, the relatively greater importance of the pneumococcus as the determining factor, and the role of cooling, which increases the hyperergic reactions but is of little influence outside the conditions of sensitization. The author points out an analogy between some of the metabolic functions of the liver and the lungs, such as the removal of excess lactic acid, and the nitrogenous and the chloride metabolism. In order to study the carbohydrate metabolism in experimental pneumonia, the author first determined the glycogen content of the liver, the muscles and the lungs of five control rabbits. A similar study was made of fifteen rabbits in which experimental pneumonia was induced by sensitization with intravenous injection of horse serum, followed by intravenous injection of a culture of pneumococcus, and by intratracheal introduction of horse serum. There was noted a lowering of the glycogen content of the liver to almost one tenth of the normal, while the muscle glycogen content showed slight increase, whereas the glycogen of the altered pulmonary tissue exceeded that of the control animals by 167 per cent. These experiments demonstrated marked alteration of liver function at the height of the hyperergic inflammation of the lungs. Tissue metabolism of the liver, of the unaffected lung and of the affected lung of nineteen rabbits was studied. There was noted a marked lowering of tissue respiration in the liver and a slight increase in glycolysis. In the pathologically altered lung there was a fall in tissue respiration and an increase in glycolysis. A diminution of respiration was likewise noted in the normal lung, a fact having a bearing on the anoxemia of pneumonia patients. Of the pneumonia patients

observed by the author, 22 per cent had an enlarged and tender liver. Many of these had urobilinuria. On the theory that the detoxication function of the liver depends on its glycogen content, the author applied insulin-dextrose therapy, first suggested by Kogan-Yasnyy in cases of lobar pneumonia. In a group of seventy-four patients with pneumonia treated by the insulin dextrose therapy, the mortality rate amounted to 5.4 per cent, while in a group of 131 patients treated during the same period on an orthodox regimen, the mortality amounted to 15.2 per cent. The author believes that the beneficial influence of the insulin-dextrose therapy is due to the improvement in the glycogen synthesis with the resulting increase in glycogen storage in the liver, which in turn increases the antitoxic function of the liver. The increased glycogen content also may exert a favorable effect on the allergic reactions.

Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

31: 3873-3980 (Aug. 5) 1939. Partial Index

Foreign Bodies in Esophagus. C. E. Benjamins.—p. 3874.
*Progestin in Repeated Abortion. M. H. G. A. Tholen and L. A. M. Stolte.—p. 3880.
Fractures of Jaw. B. van Ommen.—p. 3888.
Blood Picture in Metastatic Tumors of Bone Marrow and in So-Called Leukanemia. F. S. P. van Buchem and D. J. J. M. Hendriksen.—p. 3893.
Encapsulated Pericardial Exudate. J. H. Nauta.—p. 3904.

Progestin in Repeated Abortion.—Tholen and Stolte first review the present status of the knowledge about progesterone, the hormone of the corpus luteum, giving especial attention to its role in the preservation of pregnancy. They cite factors which indicate that a deficiency of corpus luteum hormone plays a part in habitual abortions and that the injection of this substance is a valuable aid in counteracting habitual abortion. Further they review the clinical histories of nine women in whom pregnancy usually terminated in abortion, twenty-nine pregnancies producing only two living children. After treatment of these women with progesterone was instituted, twelve pregnancies resulted in eight living births; to be sure, the authors admit that these probably cannot all be ascribed to the action of progesterone. Nevertheless, they are convinced that progesterone represents a valuable addition to the therapeutic armamentarium of habitual abortion. They think that larger doses than were employed by them might perhaps produce better results. The small doses employed at present and the defective differential diagnosis still necessitate a combination with other therapeutics such as a salt-free diet, thyroid and vitamin E.

Acta Chirurgica Scandinavica, Stockholm

82: 549-628 (Aug. 5) 1939

*Pneumococcic Peritonitis in Children. O. Haglind.—p. 549.
Congenital Bilateral Hydro-Ureter in Man Aged 22. C.-H. Hirschlaff-Hjortsjö.—p. 587.
*Pericardectomy in Fibrous Pericarditis: Two Cases. K. H. Köster.—p. 595.
Acute Porphyria Without Porphyrinuria. E. Schie.—p. 618.

Pneumococcic Peritonitis in Children.—Haglind says that genuine or cryptogenic pneumococcic peritonitis, in which the peritoneal fluid contains only pneumococci and in which neither operation nor necropsy discloses a local point of origin, has received considerable attention in different countries and so he decided to review the cases that were treated in Swedish hospitals during recent years. All of the seventy-seven patients who were the subject of his review were children less than 16 years of age. In all of the cases the diagnosis was bacteriologically verified. The majority of the patients (92 per cent) were girls and most of them were between 6 and 10 years old. The pneumococcic peritonitis seems to be a primary process in the majority of cases, for in only a small number did it appear as a secondary phenomenon to other forms of pneumococcic disorders. As regards the symptomatology, it is of especial interest that the anamnesis frequently reveals diarrheas, that the fever is high from the beginning and that the general condition is poor from the onset. The mortality of pneumococcic peritonitis is high, in the material reviewed here 66 per cent. The differential diagnosis is difficult and efforts have been made to find methods which will permit a definite diagnosis before an operation is resorted to, because a surgical operation during the acute stage of this form of peritonitis seems to increase the risk of death rather than reduce it. The author shows that exploratory puncture has been recommended by some as a diagnostic aid. In remarks about the pathogenesis he cites the various possible routes by which pneumococci might invade the peritoneum. In view of the fact that the majority of patients are girls, he considers a genital mode of infection possible; on the other hand, he shows that there is considerable evidence for an enterogenic infection. He says that in the treatment of pneumococcic peritonitis a conservative tendency has been gaining during recent years, although the debate about surgical or conservative treatment is still not definitely decided. The fact that pneumococcus type I seems to be the cause of the peritonitis in more than two thirds of the cases is of great interest for a possible serotherapy. The author further suggests that in view of the favorable results obtained with sulfapyridine in pneumonia it might be advisable to try this preparation also in pneumococcic peritonitis.

Pericardectomy in Fibrous Pericarditis.—After reviewing the literature on surgically treated cases of fibrous pericarditis and following remarks about the pathogenesis and diagnosis, Köster reports two cases in which the classic symptoms of fibrous pericarditis were present: increased venous pressure with protruding veins, coughing, ascites, enlarged liver, edemas, reduced beat volume with lowered blood pressure, small pulse, cyanosis, oliguria, exertion dyspnea, tachycardia and fatigue. Before, during and after pericardectomy the oscillations of the pulse volume were registered by means of Liljestrand-Zander's method, in which 0.7 mg. of epinephrine is injected previous to the registration of the pulse and the beat volume. This method yielded results similar to those obtained by other investigators with Grollmann's method. In the surgical treatment of the two patients, pericardectomy was preferred to Brauer's operation in spite of the fact that many regard the latter as adequate and less dangerous. In the first case, although the symptoms had existed a long time, the fibrous pericardium could be detached fairly readily and extensively and the patient's condition was much improved after the intervention; she is able to work. In the other case the condition developed rapidly after an attack of acute pericarditis; technically the operation was extremely difficult and only a small portion of the pericardium was resected. However, in spite of the less radical intervention, this patient made a more rapid and better recovery than did the first one. Following remarks about the problem of drainage in pericardectomy, the author says that after the operation the patients were treated with digitalis and morphine. He thinks that the postoperative prognosis seems to depend not so much on the size of the resected piece of pericardium as on what damage the heart has sustained under the influence of inactivity and compression and to what extent the disorder which caused the pericarditis (usually tuberculosis or rheumatic infection) has subsided. Operation during the acute stage is technically easier, but it involves greater dangers for the patient, and for this reason some authors advise against pericardectomy during the acute stage.

Nordisk Medicin, Helsingfors

3: 2133-2216 (July 15) 1939. Partial Index

Hospitalstidende

Vitamin C and Tuberculosis: II. Investigations on Resorption and Elimination of Ascorbic Acid in Patients with Pulmonary Tuberculosis. B. and E. Groth-Petersen.—p. 2141.
Keratoconus in Siblings. Viggo A. Jensen.—p. 2145.
*Investigation on Magnesium Content of Red Blood Corpuscles in Pernicious Anemia and Some Other Anemias. O. Bang and S. L. Ørskov.—p. 2147.

Magnesium Content of Red Cells in Anemias.—Bang and Ørskov state that an increased magnesium content of the erythrocytes seems frequently to follow in anemias originated because of relatively acute loss of blood and is further demonstrated in some anemias of long standing. In anemias due to hemorrhage as well as in experimental animals (Ørskov and Henriques) an increased magnesium content is believed to be a phenomenon connected with newly formed red blood corpuscles. In the majority of cases of pernicious anemia high magnesium values are present in the untreated stage and the relations approach normal values during remission. The view is thus supported that a short lifetime of red cells with concomitant increased rate of destruction is a decisive factor in the development of pernicious anemia.